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Postgraduate Medicine

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Carcinoma of the Cervix

JOSEPH HYDE PRATT*

Mayo Clinic and Mayo Foundation, Rochester, Minnesota

Seventy carcinomas in situ found among 285 malignant lesions of the cervix were treated by vaginal or abdominal hysterectomy, preserving the ovaries. Invasive cervical carcinoma and five-year results of primary surgery are considered. The incidence of metastasis to lymph nodes with and without preoperative irradiation is reported.

JOSEPH HYDE PRATT

In any discussion, one's own ideas of necessity color the subject matter, and for this reason I shall, of course, lean toward the surgical outlook and surgical results in considering cancer of the cervix. However, there must be some preliminary discussion of the methods utilized in arriving at a definite diagnosis and the background of data on which conclusions are based. For this reason I shall first review certain data on the malignant lesions of the uterine cervix seen in a single year at the Mayo Clinic.

In 1951, an average year, there were 285 patients with carcinoma of the cervix. Of these lesions, 149 were squamous cell epitheliomas, 70 were squamous cell epitheliomas *in situ* or stage 0 lesions, 20 were adenocarcinomas of the cervix or endocervix, and 46 were so wild-appearing microscopically that their nature was undetermined or they were in patients who were so ill that the diagnosis was unimportant and terminal care was the only consideration.

The 70 patients with carcinoma *in situ* form a special group. One of these patients was pregnant and after a thorough discussion of her problems and the presentation of our opinions to her, she decided to carry through the pregnancy under the care of her home physician. Another patient in this group refused operation and was treated with radium. The other 68 were treated surgically.

Two hundred and fifteen patients had invasive cancer of the cervix. Seventy-two of

*Section of Surgery, Mayo Clinic and Mayo Foundation, Rochester, Minnesota. The Mayo Foundation is a part of the Graduate School of the University of Minnesota.

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these had no treatment, but their condition was not nearly as hopeless as it might seem. Thirty-four of the 72 had been treated elsewhere and were seen for checkup. Four others interrupted their treatment at home to come to our clinic and were advised to return home and continue with their previous plan of radiation. Five patients elected to go elsewhere for their treatment, whether radiation or operation. Of the remaining 29 patients, there were 16 who, we felt, might possibly profit from palliative radiation in hospitals nearer their homes and 13 who were in a terminal state and for whom no treatment seemed to be indicated.

Therefore, of the 215 patients with invasive carcinoma there remained 143 for whom we felt definitive treatment was indicated and who were treated under our direction. It is from these cases that we derive our data. For 82 of these patients radiation was the only form of therapy utilized; this was palliative for 25 because of the extensiveness of the disease, local recurrences or the poor physical condition of the patient, while for 57 the treatment was completed and we were optimistic about obtaining a good result.

In 49 of the 143 patients radiation was followed by surgical treatment; in 41 of these we were able to carry out a satisfactory surgical procedure in conjunction with the radium and x-ray therapy. In general, this consisted of a Wertheim hysterectomy, that is, a radical abdominal panhysterectomy with dissection of the external and common iliac nodes as well as the tissues along the base of the bladder and through the obturator fossae. In 4 patients we found abdominal extension of the malignant process or else extension to the high aortic nodes beyond any feasible chance of surgical excision. The other 4 patients of the 49 were treated palliatively for relief of pain. This consisted of unilateral or bilateral chordotomy.

Only 12 of the patients with invasive carcinomas were treated by surgical means alone. Seven of these were treated in an attempt to cure the disease. Five were treated for purposes of palliation: 1 patient underwent prefrontal lobotomy and 1 chordotomy for pain, 1 colostomy for obstruction, and 2 construction of a cecal bladder and colonic stoma for huge rectovesicovaginal fistulas following radiation therapy.

Excluding the patients for whom treatment was palliative and including the primary surgical cases, we operated on 52 of 134 potentially surgical patients, giving an operability rate of nearly 40 per cent.

Diagnosis

A malignant lesion must of course be diagnosed before treatment can be started. Since the cervix is one of the more commonly encountered sites of malignancy and since it is an organ that is readily examined, physicians should be able to cut delays in diagnosis and institution of treatment to a period of days only. Attention to detail, development of an acute sense of suspicion, and recognition of the possibility of the condition even in our own families are three prime factors in diagnosing cervical carcinoma early.

Attention to detail both in the patient's history and in doing a routine bimanual pelvic examination, as well as care in inspection of the cervix are important. A menopausal patient may do many unexpected things, but she does not have daily bleeding, nor does she have contact bleeding or an odorous or even a foul discharge. These are signs of a very possibly serious condition and such patients do not need hormones—they need pelvic examinations.

Some of us were taught in medical school to put one finger in the vagina and one finger on our nose—if the cervix felt like the nose it was normal, if it was harder, it was the site of cancer, and if it was softer, then the woman was pregnant. This one-finger examination, however, is not entirely satisfactory. One finger in the rectum and one in the vagina, with the other hand on the abdomen, offers a far better and much more accurate aid to diagnosis. Then we get information not only about the cervix but also about the uterus, adnexa and rectum, and if carcinoma is present we can estimate the stage of the lesion as well (table 1). The stage of the disease must always be determined on the initial visit

TABLE 1

STAGES OF CARCINOMA OF THE CERVIX*

Stage 0	Carcinoma *in situ*—also known as preinvasive carcinoma, intra-epithelial carcinoma and similar conditions.
Stage I	Carcinoma is strictly confined to the cervix.
Stage II	Carcinoma extends beyond the cervix, but has not reached the pelvic wall. Carcinoma involves the vagina, but not the lower third.
Stage III	Carcinoma has reached the pelvic wall. (On rectal examination no "cancer-free" space is found between the tumor and the pelvic wall.) Carcinoma involves lower third of the vagina.
Stage IV	Carcinoma involves the bladder or the rectum, or both, and has extended beyond the limits previously described.

*International classification and classification recommended by the Fourth American Congress of Obstetrics and Gynecology, 1950.

and the patient kept in the indicated category if we are to compare results later, though from a prognostic point of view the surgical findings are the most accurate. After the bimanual examination, the cervix and vaginal walls should be inspected with as good light as is available and other diagnostic procedures should be carried out when indicated.

An acute sense of suspicion helps enormously. There is no way of knowing that an area of erosion is a simple erosion and not carcinoma *in situ* or even invasive carcinoma unless biopsy is done. The fact that the lesion has given no symptoms means only that there has been no breakdown and no infection of the surface epithelium. Routine biopsy of all areas of erosion and of areas of leukoplakia will reveal many unsuspected early malignant processes that are still in a stage in which there is hope of cure.

In addition, great help is available through the screening process of vaginal smears. During the past year our pathologists reported some 100 vaginal smears that were suspiciously positive or definitely positive for malignant cells, and the diagnosis of malignancy was confirmed in all but one or two cases. The pathologist, when studying the office biopsy specimens, has only tiny bits of tissue and therefore is careful not to state definitely that the lesion is *in situ* in all areas. From biopsy, therefore, he reports the lesion as "carcinoma of the cervix, apparently *in situ*."

The patient then undergoes biopsy under anesthesia. The surgical biopsy specimen represents practically a conization of the central cervical and endocervical regions in order to get the important squamocolumnar junction. Frozen sections are made and studied immediately and are reported as showing either carcinoma *in situ*, invasive carcinoma, or no evidence of residual carcinoma. Occasionally, light cautery to control bleeding results in enough destruction of the surface layers of the cervix to cause the pathologist to find no identifiable carcinoma remaining and the lesion remains classified as carcinoma *in situ*.

Treatment

When surgical biopsy shows no invasion, our preferred treatment for carcinoma *in situ* is hysterectomy including removal of a cuff of vaginal mucosa but with preservation of the ovaries. We see no necessity of doing an abdominal hysterectomy if the vaginal approach can be used satisfactorily. This means sufficient relaxation and descensus to make vaginal hysterectomy fairly easy without having to pull on the cervix unduly or hemisecting the uterus.

When invasive carcinoma of the cervix is identified our treatment varies widely and radically from the treatment of carcinoma *in situ*. For a number of years, for early lesions

we employed primary Wertheim hysterectomy without preoperative radiation. We still do this in a few cases when the lesion is very small and early, when it begins in a cervical stump with possible adherent loops of bowel, or when an ovarian lesion or the anatomy of the vagina contraindicates the use of radium.

With the exception of the foregoing conditions our present plan is to treat invasive carcinoma of the cervix with radium and deep x-rays and to follow this in suitable cases with a radical hysterectomy. In the average case, radium therapy consists in the placement of radium into the uterine canal and vagina for a total of approximately eight treatments. A total treatment of about 7300 mg. hours results in the delivery of 6500 to 8000 gamma roentgens to point A and 1800 to 2500 gamma roentgens to point B. Concurrently with the radium treatments the dose to the parametrium is supplemented by external roentgen therapy using two anterior and two posterior fields to deliver an additional dose of 2000 to 2500 roentgens to the midplane of the pelvis. The patients are then allowed to go home and are asked to return in three months, when an evaluation is made by the radiologist, the surgeon and the gynecologist and a decision reached regarding surgical treatment.

There is considerable difference of opinion as to how effectively the lymph nodes of the pelvis are attacked by the use of radiation. Some men feel that cancer in the pelvic nodes cannot be eradicated by x-ray therapy but most believe that at least some beneficial results are obtained. In our own cases, the evidence suggests that the pelvic nodes are not sterilized by radiation—24 of 171 patients with no preoperative radiation had involved nodes while 25 of 122 patients with preoperative radiation had such nodes.

Choice of Patients for Operation

The choice of patients for operation following irradiation is on the basis of both exclusion and inclusion. We immediately exclude those with distant metastasis, the elderly whose physiologic age is more than 60, the poor-risk patients with little cardiac reserve and so forth, and a large group of obese patients. The need for reduction of weight is stressed to all the overweight patients and diets are prescribed, but the number that do not carry through on this program is distressingly large.

We include all reasonably healthy patients and select first those whose lesions are radioresistant as indicated by the positive evidence of biopsy or the suggestive evidence of a poor clinical response to the radiation.

We feel that surgical treatment is indicated for stage I and stage II lesions; it is also indicated for stage III lesions if there is any freedom laterally to indicate possible cleavage planes on the sides of the pelvis.

Invasion of the bladder or rectum does not contraindicate surgical treatment but if such treatment is to be considered it must include parts or all of the invaded organs, with some increase in risk and morbidity. Pain in the flank with radiation to the legs is a very bad prognostic sign and often indicates metastasis to the lumbar plexus. Enlargement of the uterus is encountered not infrequently after radiation and generally means pyometra from cervical stenosis; occasionally there is extension of the original growth into the uterus.

Mortality and Morbidity

When we advise surgical treatment we discuss with the patient the risk, the morbidity and to some extent the complications. The surgical mortality rate has been remarkably reduced through selection of patients and the use of blood, blood substitutes and intravenous fluids. Thus, in several large recent series a rate of less than 3 per cent is reported, whereas in Bonney's[1] and Wertheim's series it ranged upward from 14 and 19 per cent, respectively. Among our patients from 1930 through 1952 there were 293 Wertheim hysterectomies with 9 deaths, giving an over-all fatality rate of 3.1 per cent, but since the last death in 1943 there have been well over 200 consecutive Wertheim hysterectomies without a death.

These patients spend an average of two weeks in the hospital after operation, and our greatest difficulty is with the urinary tract.

Retention causes considerable distress. We routinely leave a Foley catheter in the bladder for five days, and then catheterize the patients twice daily until the residual urine is 50 cc. or less. If we find large residuals, we replace the catheter for one to two days and then remove it again. In most cases the retention clears up within two weeks but occasionally it persists as long as three weeks.

Urinary fistula is a most exasperating complication, for one feels that it should be preventable. We had 12 such fistulas in 293 patients, giving a rate of about 4 per cent. There were 3 ureteral fistulas, all necessitating reoperation, and 1 rectovesicovaginal fistula, 1 rectovaginal fistula, and 8 vesicovaginal fistulas. Surprisingly, 4 of 8 vesicovaginal fistulas healed spontaneously and only 3 had to be repaired.

Results of Treatment

The results with carcinoma *in situ* have been most satisfactory in that so far there have been no recurrences of which we are cognizant, nor have there been implantations in incisions along the vaginal canal. Admittedly, there has been no accurate and orderly follow-up of these patients, since the great majority have been treated in only the last four to five years.

Many of these patients also have a large cystocele and rectocele, and with the evidence of the very slight possibility of recurrences or implantation we repair the cystocele or rectocele if either is giving bothersome symptoms, although our preference is vaginal hysterectomy without associated repairs.

When invasive carcinoma of the cervix is treated by radiation alone, the results vary from clinic to clinic. Bowing and Fricke[2] reported an over-all five-year survival rate of 32.8 per cent for patients who had had their treatment here in Rochester; this rate is based on 1,581 patients. Heyman of Stockholm reported a five-year survival rate of 37 per cent on the basis of 1,224 patients, and Corscaden[3] reported a five-year survival rate of 43 per cent on the basis of 149 patients. These results included all the patients who had completed their treatment during a given period at the institution reporting them, and the reports of necessity included a rather high percentage of stage III and stage IV lesions.

Surgical treatment alone for invasive carcinoma of the cervix has not had many advocates through the years, although the pendulum now seems to be swinging back toward such treatment or toward a combination of radiation and surgical treatment. Bonney has long been an advocate of primary surgical treatment without preoperative or postoperative radiation. Although he had a primary mortality rate of 14 per cent, he did get a five-year survival rate of 40 per cent. His incidence of affected lymph nodes was also 40 per cent.

At the present time we are attempting to compare our results from surgical treatment alone with our results from radiation followed by surgical treatment. Although we can not compare random series of patients, since the percentages in the different stages would vary markedly and therefore the final results would be entirely different, we can compare series of patients if the lesions are of similar stage; that is, we can compare stage I with stage I, stage II with stage II, and so forth. We are gradually acquiring the experience and the number of patients to allow us to do this. These patients will all have been examined and the stage determined by the same group of men.

From 1930 through 1949 we treated most of the invasive carcinomas of the cervix by radiation alone, but a selected group of stage I and stage II lesions and a few stage III lesions did receive primary surgical treatment. A follow-up study on the first 122 of these, with 9 hospital deaths, published elsewhere,[4] shows an over-all five-year survival rate of 79.8 per cent based on 109 traced patients (table 2). When we divide this group according to stage of disease, we find that of 72 traced stage I patients, 84.7 per cent survived five years, and that of 29 stage II patients 82.8 per cent survived five years.

The surgical approach gives a tremendous prognostic advantage in that it reveals the status of the regional lymph nodes, which along with the stage of the disease as deter-

TABLE 2

SURVIVAL RATES AFTER WERTHEIM HYSTERECTOMY FOR SQUAMOUS CELL EPITHELIOMA OF THE CERVIX*

PERIOD, YEARS	PATIENTS		LIVED BEYOND INDICATED PERIOD	
	TOTAL	TRACED	NUMBER	PER CENT†
3	135	130	112	86.2
5	113	109	87	79.8
10	56	55	36	65.5

*Inquiry as of January 1, 1951. Included in the three-year group are only those patients who were operated on three or more years prior to the time of inquiry, that is, in 1947 or earlier; the five-year group includes those patients operated on in 1945 or earlier; and the 10-year group includes patients operated on in 1940 or earlier. Hospital deaths are excluded in the calculation of survival rates.

†Per cent of traced patients.

mined on the initial visit offers the most important single clue as to the patient's survival. When this group of 109 patients is again studied on the basis of involvement of lymph nodes, we find that of those in stage I without affected nodes, 89.2 per cent survived five years, and that of those in stage II, 86.4 per cent survived five years. Those with affected nodes are too few to be of statistical interest, but 3 of 7 in stage I and 5 of 7 in stage II lived five or more years. Only a few of the first 122 patients had affected nodes; later, as more patients with such nodes can be included in the five-year postoperative studies, our five-year survival rate probably will approach closer to the rate of 21 per cent reported by Bonney on the basis of 200 patients with affected nodes.

In 1949 we made a basic change in treatment and decided to try for a period of several years to treat all our patients preoperatively with radium and deep x-rays. We would then have two groups, comparable as to stage of the disease, from which we might be able at least to observe the effects of preoperative radiation (1) on survival, (2) on the incidence of involved lymph nodes and (3) on complications and postoperative morbidity.

We have no five-year groups to compare yet but we do have some interesting figures on the numbers of involved lymph nodes. We found that with no preoperative radiation 8.4 per cent of patients in stage I and 24.4 per cent of those in stage II had involvement of nodes while with preoperative radiation 11.6 per cent of patients in stage I and 23.9 per cent in stage II had involvement of the nodes. Evidently little has been accomplished by our radiation to the sides of the pelvis.

Summary and Conclusion

This paper deals primarily with the cases of carcinoma of the cervix encountered in a typical year at the Mayo Clinic. We feel that carcinoma *in situ* represents a very early stage of true invasive carcinoma of the cervix and we recommend hysterectomy with preservation of the ovaries; either the vaginal or the abdominal approach is used, depending on relaxation, descensus and the size of the uterus. Radiation is the foundation stone of our treatment of invasive carcinoma of the cervix at present but in selected cases, approximately 40 per cent of the total, we follow the radiation in three months with Wertheim hysterectomy.

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Duodenal Diverticulo-Jejunostomy

R. ROBERT DE NICOLA*

Kadlec Hospital, Richland, Washington

Diverticula of the duodenum rarely cause symptoms unless they are large, fill easily and remain distended. Previously described surgical methods seem needlessly radical or include the risks of recurrence or damage to the ampulla of Vater. Duodenal diverticulo-jejunostomy is offered as an alternative procedure when excision seems unsafe.

R. ROBERT DE NICOLA

SINCE 1915, when Försell and Key[1] first removed a diverticulum of the duodenum, many surgical technics for the relief of symptoms arising from this abnormality have been described. Although there has been general agreement that correction must be directed simply toward elimination of diverticulum pooling,[1-8] the procedures advised have been impressively and needlessly radical. Thus one finds advocates of complete inversion,[4,9] diverticulum excision, diverticulum excision with sidetracking operations or common duct drainage with long T tubes,[3] subtotal gastrectomy,[7] and even excision of the duodenum involved, with gastroenterostomy and reconnection of the biliary pathway.[10,11] A further indication of the extent of surgery advocated in these cases is demonstrated by the complicated triple operation of Bartlett, who in three patients occluded the pylorus with fascia lata, did a gastroenterostomy and finally a vagotomy to prevent marginal ulcer.[12] The main reason for the difficulty in finding a simple solution to this problem appears to be the frequent close anatomic relationship of the duodenal diverticula to the ampulla of Vater. As a matter of fact, Collett et al. clearly demonstrate one case in which the common duct entered the diverticulum proper.[13]

A consideration of the mechanical effects of diverticulum distention in relation to the symptoms produced is important. The distention, either alone or by pressure on the duodenum itself, may cause the most common symptoms which are abdominal pain and nausea. These symptoms in turn are associated

*Department of Surgery, Kadlec Hospital, Richland, Washington.

with fear of eating which results in the marked weight loss invariably associated with symptomatic duodenal diverticula. Beyond this, there are few problems attributable to the uncomplicated diverticulum. Diarrhea from pancreatic disturbance,[14] perforation from diverticulitis,[15] and hemorrhage or carcinoma of the sac[11] are extremely rare. The main practical consideration, then, is to prevent filling and retention in the pouch without endangering the proximal biliary flow.

Inversion of the diverticulum gives rise to the possibilities of (1) recurrence, (2) the accumulation of gelatinous mucoid material inside the inverted sac,[16] and (3) partial duodenal obstruction from "bulk" and/or an encroachment on the ampulla of Vater.

Sidetracking the abnormality may not affect the symptoms of the retained diverticulum which is free to fill with ingested material and form bezoars.[6]

Excision of the sac is the most direct approach and should be done in most cases, but is not necessary, as the symptoms are not caused by the existence of the sac alone, but by its inability to empty. Therefore, when the diverticulum is close to the ampulla of Vater, as in most cases, excision is not always the indicated safe procedure.

With these anatomic factors in mind, in addition to the knowledge that jejunal diverticula rarely give symptoms as they are almost "unfillable,"[7] when presented with a large "perivaterian" duodenal diverticulum I anastomosed it to the proximal jejunum. In this direct manner the symptoms of diverticulum retention were relieved without the risks of more radical surgery.

Case Report

The patient, a 38 year old Negro woman, was admitted to the Kadlec Hospital on July 23, 1951, with the chief complaint of recurrent abdominal pain. This symptom had been present for the past three years and had caused considerable clinical investigation during this time. After a diagnostic study at a distant clinic the patient had been discharged to a local physician for psychiatric treatment. The patient developed a fear of eating and a weight loss of over 20 pounds had occurred during the 18 months prior to admission. Physical examination revealed a well-developed but thin woman who was depressed and appeared chronically ill. There was mild tenderness above and to the right of the umbilicus but no spasm. No abdominal masses or organs were palpable. The blood count and other laboratory studies revealed nothing abnormal. X-rays showed a large, somewhat bilobate diverticulum arising from the descending or second portion of the duodenum (figure 1), which almost completely retained barium (figure 2). No other abnormalities were demonstrated.

The patient underwent surgery on July 25, 1951. Exploration revealed a normal stomach, pylorus and duodenal bulb. The gallbladder and pancreas were also normal. The duodenal diverticulum could be seen as a large sac projecting upward and to the right, just lateral to the common duct. The diverticulum was easily dissected to a wide neck and its distal portion was approximately 6 cm. in diameter. Although the sac wall appeared and felt much thinner than the intestine from which it arose, it was nevertheless a firmly lined structure covered with serosa. It occurred to me at this time that the only pathology arising in connection with this sac was its tendency to fill with ingested material, which remained trapped within it and caused symptoms by pressure on surrounding structures. Because of this and its proximity to the exit of the common bile duct, it was decided that treatment could be directed at simply allowing the diverticulum to empty adequately and rapidly whenever it became filled. Accordingly, a two-layer anastomosis was made of the entire width of the duodenal diverticulum with the jejunum, approximately 15 cm. from the ligament of Treitz. The jejunum was attached to the fixed duodenum on each side of the anastomosis.

There has been a most gratifying therapeutic result in this patient. She was discharged from the hospital eight days following the operation and the previous discomfort has not recurred. She eats normally without fear of pain or nausea and has returned to her previ-

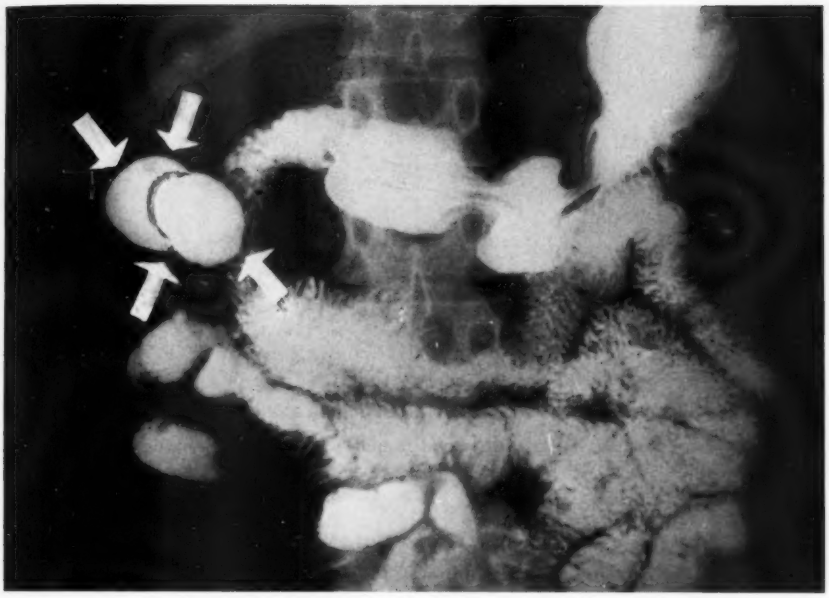

FIGURE 1. Gastrointestinal series revealing a large diverticulum arising from the second portion of the duodenum.

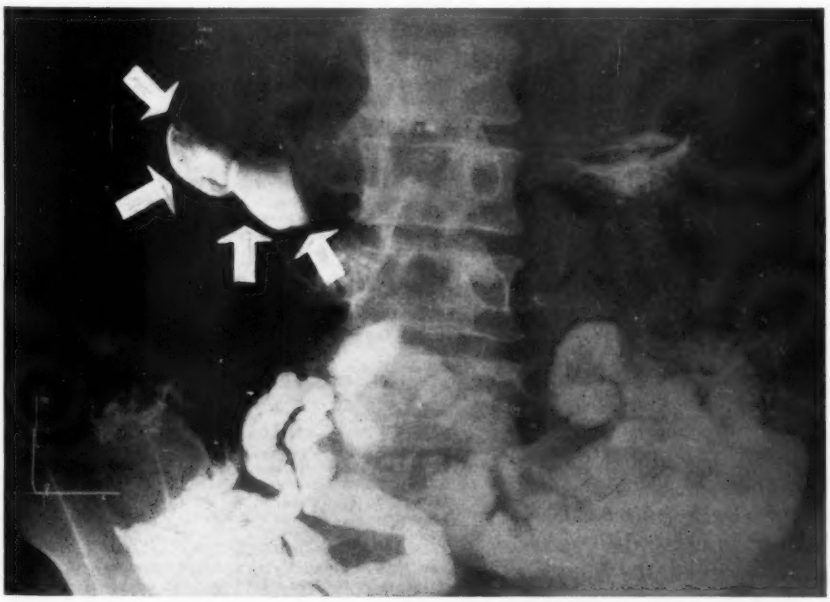

FIGURE 2. A six-hour plate showing extensive barium retention in the duodenal diverticulum.

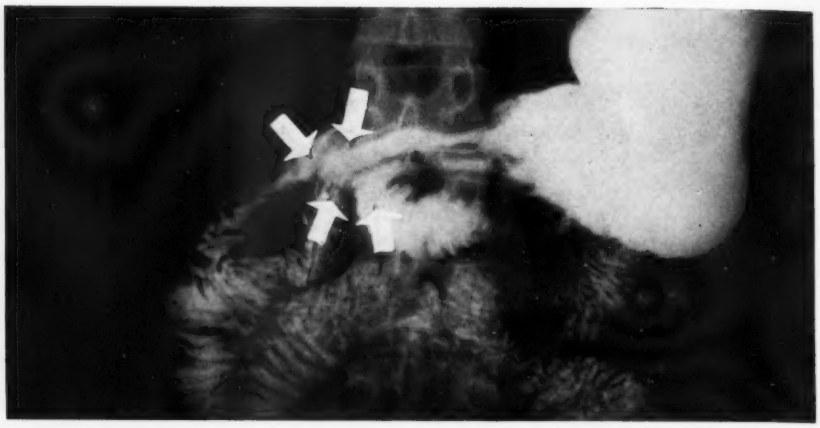

FIGURE 3. Gastrointestinal series taken several months postoperatively showing rapid emptying through the duodenal diverticulo-jejunostomy.

ous occupation. Barium x-rays several months following operation revealed rapid emptying of the barium into the jejunum (figure 3). There has been such a marked weight gain (over 50 pounds) in the two years following the duodenal diverticulo-jejunostomy that a reducing diet was instituted at the patient's last clinic visit.

Comment

The simplicity of this procedure should make it a practical consideration whenever attention is directed to relieving symptoms from duodenal diverticula. It leaves the duodenal coil and biliary relationship in a completely normal state and avoids the dangers of compression of either system. The anastomosis procedure does not contain the dangers of marginal ulcer as the acid component of a gastroenterostomy is not present. There may be instances in which the site of origin and direction of the diverticulum would make such an anastomosis awkward and in these cases the diverticulum should perhaps be carefully excised. However, even a posterior origin on the second or third portion of the duodenum may permit a satisfactory retrocolic duodenal diverticulo-jejunostomy. In cases where much of the diverticulum is buried in the pancreas it might well be practical to avoid total dissection, with injury to the pancreas, in favor of partial dissection adequate for jejunal anastomosis. The serosal covering of the diverticulum heals well to the serosa of the jejunum but perianastomotic duodenojejunal sutures will safeguard the line of anastomosis and at the same time relieve the diverticulum of the jejunal weight.

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Postoperative Thyroid Storm

TIMOTHY A. LAMPHIER AND
WILLIAM WICKMAN

Boston, Massachusetts and Miami, Florida

This paper is a short treatise on the present status of postoperative thyroid crisis as regards theories, etiology, symptomatology and methods of treatment. The point is stressed that in spite of present day antithyroid preoperative medication, this grave condition may still occur. The accompanying high mortality rate can be avoided by immediate treatment. Three cases are reported in which there occurred one death. The theory is postulated that this complication may be anticipated in patients with extremely high initial basal metabolic rates.

THE syndrome known as thyroid storm or crisis, although frequently encountered in the early days of thyroid surgery, is not often observed today. This is due to more adequate preparation of toxic patients for surgery with the thiouracil group of drugs. The incidence of postoperative storm has greatly decreased, although it is far from being extinct.[1] It still occurs under the best of conditions, even with prolonged preoperative hospital preparation.

This paper deals with three cases of postoperative thyroid storm, one of which ended in a fatality. The purposes of this paper are: (1) to emphasize the fact that postoperative storm may occur even with adequate preoperative management and in spite of present preoperative antithyroid medication; (2) to review the symptoms of thyroid storm, and (3) to review the present day treatment of this condition. "Thyroid crisis is a syndrome of many facets and not a specific entity."[1] The prompt recognition of this most fearful postoperative complication is essential to avoid undue mortality. Death in this state results from the various complications which are associated with increased metabolism and which often are inadequately treated. We know that patients experiencing medical storm are much more toxic than those having surgical storm. Indeed, the mortality rate for medical storm is close to 100 per cent. The treatment thereof is ineffective. Although we fail to understand the underlying physiologic principles of this syndrome, it is essential that we sense its presence at once so that we may give emergency treatment to control it.

Many surgeons today complete their entire surgical training without encountering this phenomenon. "Thyroid crisis is not a specific entity, but rather the sum total of the effects on the many body systems of a fulminating thyrotoxicosis."[2] McArthur[1] and others have defined thyroid crisis as a "life-endangering augmentation of the symptoms of thyrotoxicosis in which the patient's response is out of proportion to the exciting stimulus." Effective antithyroid agents and improved surgical technics have greatly diminished the incidence of thyroid crisis.[2] Rives and Shepard[3] stated: "We were impressed with the fact that the com-

plete failure of the heat-regulating mechanism in these cases is strikingly similar to that seen in heat stroke." Thyrotoxicosis causes increased heat production and humidity, and high temperature renders elimination difficult, thus increasing the hazards materially. As stated, when thyroid storm occurs without any exciting factor, the condition is most difficult to treat and all but impossible to control.

TIMOTHY A. LAMPHIER

WILLIAM WICKMAN

Even though the cause of thyroid storm cannot be controlled, we should be prepared to treat every symptom of thyroid storm in order that we may be able somewhat to bridle it. In the past three decades, thyroid crisis has caused the death of about one per cent of all thyrotoxic patients.[2] The mortality rate of thyroid crisis itself in some series is as high as 66 per cent.[2] "Of the total number of thyroid storms (total 36) that have occurred at the Massachusetts General Hospital in the past 25 years, 25 of these storms have been surgical with a 64 per cent mortality."[1] In another series of 19 crises precipitated by operation, reported by Rives and Shepard,[3] there were four deaths or a mortality of 21 per cent.

Thyroid storm is a condition characterized by uncontrolled hyperthyroidism. This complication may occur prior to an operation but usually happens postoperatively. All the symptoms of thyrotoxicosis are markedly exaggerated and disproportionate to the stimulating factor. As McArthur et al.[1] point out, thyroid storm essentially represents the inability of the patient to adjust himself any longer to the strain imposed by the hyperthyroidism and might be called decompensated thyrotoxicosis. Under these circumstances, it is impossible to determine the basal metabolic rate, and nothing but a spurious result could possibly be obtained, because of the patient's extreme restlessness.[4] In all probability, the oxygen consumption and heat production become far greater than in any other disease known. From both the pathologic and physiologic points of view, no one as yet has been able to explain the mechanism of thyroid crisis. There are no pathognomonic features which are common to all cases.

"From the correlation of the clinical and postmortem studies, there is not sufficient proof to indict the heart as the primary site of the difficulty in patients in whom thyroid crisis develops. Certainly, such patients may die a so-called cardiac death, but in the absence of specific myocardial lesions, it is safe to assume that perhaps failure is on a physiologic rather than pathologic basis."[4] The many cases reported to date indicate that the symptoms of thyrotoxicosis are progressively augmented as they pertain to each of the great body systems (central nervous, cardiovascular and hepatorenal systems), until death or recovery takes place. Clinical and necropsy findings disclose a breakdown of one of these main body systems. Findings at autopsy are not uniform or pathognomonic in all cases.

The deaths in thyroid crisis are frequently "cardiac deaths," at least terminally, and this aspect has received universal attention. There are three opinions concerning thyroid disease and the heart: (1) Thyrotoxicosis has no effect on the heart except to increase the metabolic activity; (2) thyroid disease causes myocardial damage, hypertrophy of the heart and various clinical cardiac manifestations, and (3) thyrotoxicosis acts only as a catalytic agent and brings to the surface latent cardiovascular lesions.[5]

The clinical and experimental studies carried out by Goetsch and Ritzmann[6] indicate that the hyperthermia in thyroid storm is due to the action of epinephrine, the effect of which is probably enhanced in cases of hyperthyroidism.

It was not until the mid-thirties that the role of the liver was appreciated. Autopsy, as stated by Beaver and Pemberton,[7] will reveal

three predominant types of lesions in the liver following death due to thyroid storm: (1) acute degenerative lesions (fatty metamorphosis, focal and central necrosis, and changes secondary to stasis of blood; (2) simple atrophy, and (3) subacute atrophy (toxic) and toxic cirrhosis. "The liver changes just described can be reproduced by anoxia of an anoxic type in experimental animals in apparent hyperthyroid state. Correlation may be more than fortuitous. At the present time, it would seem to us that the hepatic changes occurring in patients with hyperthyroidism and thyroid crisis may well be explained on the basis of chronic anoxia in an organ already showing an increased oxygen consumption and glycogen depletion."[5]

The outstanding manifestation of thyroid storm is the apparent failure of the heat-regulating mechanism in the body, and this is usually associated with a rapid pulse, flushed face, profuse sweating and extremely cold extremities, and an elevated temperature. The body temperature generally rises above 103° F. and may even rise as high as 107° F. The pulse ranges from 120 to 160 per minute or faster. Quite frequently, it races so fast that it is imperceptible. The patient exhibits extreme restlessness and becomes very apprehensive. Talkativeness merges into delirium. The terminal picture is one of delirium psychosis, coma and death. Occasionally thyroid storm is characterized by nausea, vomiting and diarrhea, in addition to those symptoms already listed.

Thyroid storm may be initiated by many factors. A fatal case of thyroid crisis following injection of varicose veins was reported by Greene and Greene.[8] Thyroid storm following an operation usually begins about six to eight hours after surgery and may last from six to eight days; in the majority of cases it lasts from two to five days. Ransom and Bayley[9] found that 8 out of 10 deaths occurred within two days after the onset of crisis. They feel that if a patient survives the first 48 hours of the storm his chances of survival are good. As stated by Fiske,[10] pain, slight hemorrhage, emotional stress, injection of ADRENALIN®, foreign and split proteins (operative tissue injury) may cause this dreaded condition.

Preoperatively, it is not sound judgment to rely on a single recording of metabolic rate, for frequently patients who are highly toxic will be found to have comparatively low basal metabolic rates.

Basal metabolic rates may be determined with administration of I^{131} and a Geiger counter. I^{131} accumulation gradients indicate iodine uptake and turnover in the thyroid gland. Serum protein bound iodine indicates the quantity of circulating thyroid hormone. Clinical judgment and experience will determine the opportune time for operation. As stated by Greene and Greene,[11] the following criteria should be met before surgery is carried out:

1. The weight curve must be rising.
2. The pulse rate must be approximately normal.
3. Nervousness, apprehension and emotional instability must be adequately controlled.
4. The metabolic rate must have fallen, preferably to below plus 20, prior to surgery.

Occasionally, the patient becomes so restless in thyroid storm that he is held in bed only with considerable effort and frequently requires mechanical restraints. If the condition is not adequately treated, marked dehydration takes place and the pulse continues to rise. Auricular fibrillation with a marked pulse deficit will set in. As seen in figure 1, although the actual mechanism inducing thyrotoxicosis is not known, excessive handling of toxic hyperplastic tissue at operation, liberating large amounts of thyroxin into the blood stream, has been hypothesized as a basic cause for this condition.

However, we have no accurate knowledge of what actually incites thyroid overactivity and any theory is mere conjecture. Whenever a patient claims that he has had a loss of 50 pounds or more, certainly we should consider this patient as a possible candidate for postoperative thyroid storm.

As has been stated, the etiology of this syndrome is still unknown. In spite of extensive physiologic and pathologic search of the nervous, cardiovascular and hepatorenal systems, the thymus and adrenal glands, and chemical analysis of certain elements in the circulating

body fluids, no conclusion has been reached.

Crile[12] has pointed out that the known precipitating factors of thyroid disease (fear, anger, worry, infections, operations, pain, asphyxia, hemorrhage and physical exertion) are factors stimulating the adrenals.

"In spite of the considerable amount of information regarding physiologic interrelationship between the thyroid gland and the pituitary-adrenal endocrine system, the understanding of the aberrations and the clinical manifestations of this relationship is still quite deficient."[13] Corticotropin has been used in the treatment of some of these cases but since the pathogenesis of thyroid storm is not understood, it cannot be advocated as treatment per se.

Hill et al.[14] compare the clinical picture of thyroid crisis to the stress reaction that, in turn, forms a part of Selye's adaptation syndrome and is intimately interconnected with the pituitary-adrenal system. They ask the question: Can thyroid crisis be the emergence on a clinical level of a sudden loss of balance between the stress of hyperthyroidism and the antistress defense of the pituitary-adrenal excess? The relationship cannot possibly be substantiated since thyroid crisis cannot be reproduced experimentally. However, they do point out that not only corticotropin but also adrenal corticoids of various types do inhibit thyroid function. They also point out that the basal metabolic rate is not a reliable index of thyroid function when corticoids are being administered or their production is being stimulated, as they are calorigenic. Hypokalemia must also be combated. Hypertrophy of the adrenal glands in hyperthyroidism and their atrophy in athyreosis have often been noted. They further theorize that if thyroxin production is high, but accompanied by an adequately increased adrenal-cortical output, one deals with a state of compensated hyperthyroidism, a concept recognized by others as well. It is postulated that if the cortical response lags behind increased thyroxin output, the state of hyperthyroidism eventually becomes decompensated, and the picture of thyrotoxicosis appears.

Surgery was decided on as the procedure of choice in the treatment of the following three cases in view of the extreme initial toxicity present and the rather large number of recurrences in patients treated by either radioactive iodine or propylthiouracil. With antithyroid drug treatment, 50 per cent do not remain in the euthyroid state after discontinuance of the drug.

Case 1—This 23 year old white man was first seen at the Massachusetts General Hospital, Boston, on January 8, 1952. He gave a history suggestive of thyrotoxicosis in addi-

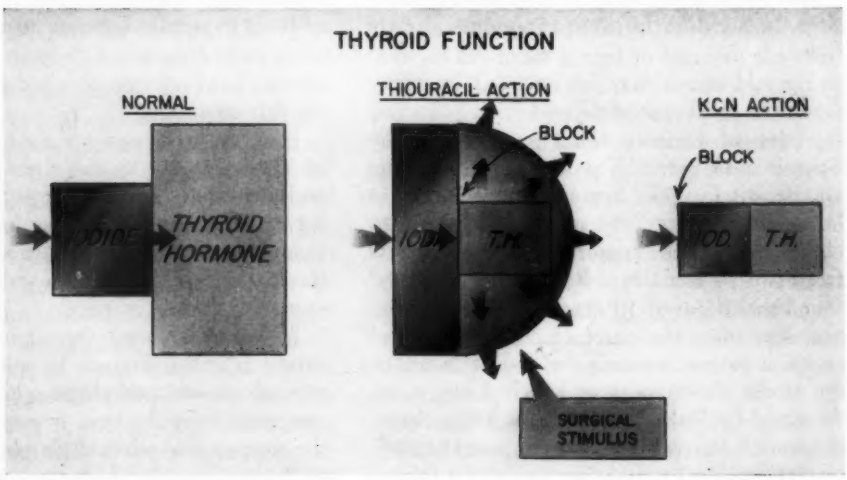

FIGURE 1. Artist's conception of the sudden and generalized liberation of thyroxin via surgical stimulus in spite of adequate thiouracil preparation. Subsequent production of thyroid crisis results.

tion to a history of hypertension for about one to two years, for which he had been rejected by the armed services. Prior to that time in his estimation his physical condition was perfectly normal. He had been told by an army physician that he had a goiter, and he had then reported to the Massachusetts General Hospital where his basal metabolic rate was found to be plus 90. He was started on antithyroid therapy, TAPAZOL®, 10 mg. three times a day. He discontinued treatment at the hospital on April 5, 1952, at which time his basal metabolic rate was still elevated, plus 56, and he still appeared to be toxic. His weight had increased to 181½ pounds, or a total gain in weight of 20 pounds.

In September 1952 he was first seen by one of the authors (T. A. L.) at the Brusch Medical Center at which time his basal metabolic rate was found to be plus 60 and his weight was 153 pounds. His blood pressure was 230/150. He was given propylthiouracil, 300 mg. daily, which was found to be inadequate after one month's treatment; subsequently this drug was replaced by Tapazol combined with phenobarbital. The patient was advised to omit all smoking and carbonated beverages and to rest for several hours a day. His basal metabolic rate gradually subsided until it was plus 6 on December 1, 1952, with a weight gain of 40 pounds, and he was considered ready for surgery.

Physical examination revealed a well-nourished, well-developed man who appeared to be his stated age. He was quite nervous and perspired freely. The skin was moist and clammy. There was a definite lid lag with a stare and some difficulty with convergence. Positive von Graefe's, Stellwag's and Möbius' signs were present. The fundi were normal. There was a 4 plus enlarged goiter of the right lateral lobe with a 2 plus enlargement of the left lateral lobe with a definite bruit. The masses were quite firm to palpation and their surfaces were smooth. The enlargement described included both the lateral lobes and the pyramidal lobes. The masses moved with deglutition and there were no associated nodules. The consistency of the goiter seemed to be rather firm; the lungs were clear, and there was a grade 2 apical systolic murmur. A_2 was greater than P_2. The blood pressure was 170/90, the pulse 120, but regular. Two repeat basal metabolic rates were within normal limits.

The patient was admitted to the Otis General Hospital on December 11, 1952, and on the following day an attempt was made to intubate the patient for thyroidectomy. This attempt failed because of marked deviation of the trachea to the left. The anesthetist's comment was that he had never seen such marked deviation, and in spite of direct vision with the laryngoscope, and even blind intubation, all attempts failed. On December 15 a second attempt at intubation succeeded.

A subtotal resection of the lobe was performed. During the procedure, bleeding became so excessive because of a generalized ooze that the operation was delayed for one-half hour and a "cut-down" carried out on the right saphenous vein for rapid infusion of whole blood. During this time, the patient's blood pressure could not be obtained, and his general condition was very poor. Some GELFOAM® pads were applied to the right side of the neck to control a persistent ooze. A dry, sterile, pressure-type dressing was applied to the wound. The patient was returned to his bed in only fair condition because of a persistent extremely low blood pressure, an elevated pulse and markedly elevated respiration.

Gross description of thyroid specimen: The specimen consisted of many fragments of tissue, the aggregate mass of which measured 10 by 8 by 4 cm. After FORMALIN® fixation the total mass weighs 180 gm. The largest single piece measures 8.5 by 4 by 3.5 cm. Cut section of the thyroid tissue had a beefy-red color. Nodularity could be seen in only a few small places in which the surrounding tissue was fixed in Formalin. Cut sections through all the fragments of tissue revealed the same beefy color. No well-defined nodules were seen in the gross or cut section. Microscopic diagnosis: Primary hyperplasia of thyroid showing no iodine effect.

Immediately following surgery the patient's temperature rose to 105.4° F., and there developed a typical thyroid storm. The patient was nonresponsive, cold, sweating profusely,

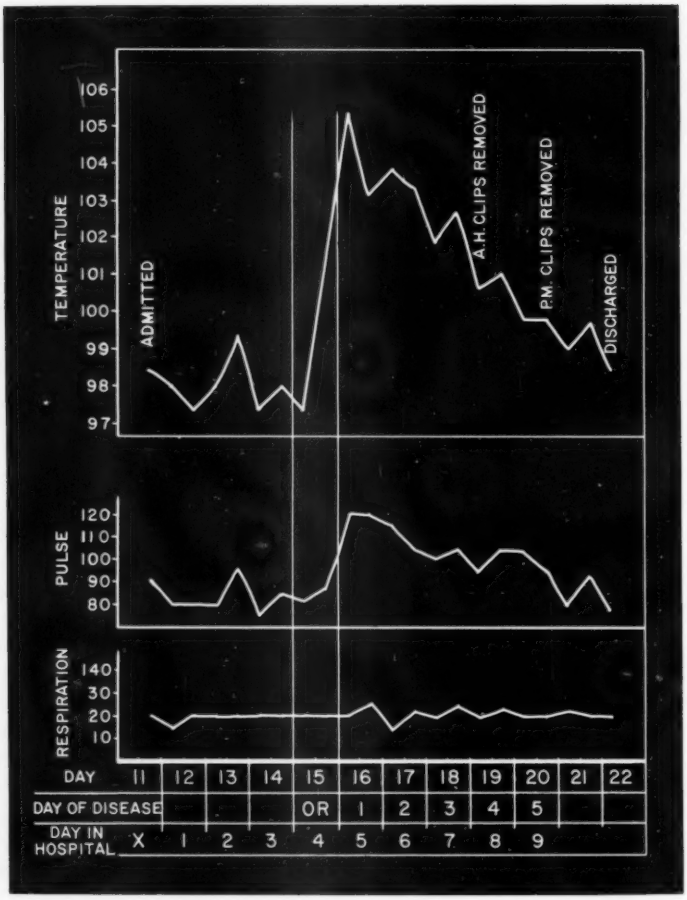

FIGURE 2. Temperature chart of patient in case 1.

and at times the pulse was so rapid that it could not be counted. At other times he appeared delirious and incoherent. His treatment consisted of: (1) NEMBUTAL® intravenously; (2) by Levin tube 30 gr. of chloral hydrate, administered every time the patient stirred; (3) morphine sulfate, ¼ or ⅙ gr. every four hours; (4) oxygen tent; (5) glucose solution or KARO® syrup or chocolate milk via Levin tube; (6) Lugol's solution, 30 drops intravenously, once a day, or 10 drops in tap water by rectum, three times daily; (7) Lugol's solution, 10 drops, three times daily, by mouth in chocolate milk. On the third postoperative day he became rational and improved rapidly. His temperature returned to normal limits, and from then on his postoperative course could be termed normal.

At the onset of the thyroid storm, he was seen by a medical consultant who simply stated that the patient had a thyroid storm following thyroidectomy and recommended routine treatment. An electrocardiogram showed no marked abnormalities present except for A and V rates. During the week immediately following surgery, as shown in the temperature chart (figure 2), the temperature gradually dropped to normal, and he was discharged

improved on his seventh postoperative day.

One week postoperatively, there was found a large collection of serous fluid in the neck which was probed and the fluid liberated at the lateral pole of the wound.

Six months postoperatively his basal metabolic rate was reported as plus 15. The patient's weight was reported as 198 pounds, blood pressure 160/90, and he stated that he had returned to work and that his progress had been excellent.

Case 2—A 41 year old patient (white man) was admitted to the New England Sanatorium Hospital, Boston, on August 14, 1949 with complaints of loss of weight, precordial palpitation, extreme nervousness and sweating. Symptoms had persisted for a period of five weeks, except for the sweating which had begun about six months before.

His local physician previously had ordered a basal metabolic test which was reported as plus 86. He was immediately placed on propylthiouracil, 300 mg. a day. His basal metabolic rate taken one month later was reported as plus 46, and following another month as plus 22. For three weeks prior to admission to the hospital, he had been prepared not only with propylthiouracil but also with Lugol's solution, 10 drops, three times daily. He had also been given large doses of calcium and vitamins. He stated that he had been especially fond of sweets for three or four months before entering the hospital.

Physical examination revealed a small, thin man who appeared to be of the stated age. There was a moderate exophthalmos with some lid lag. Pupils were round, regular, equal and reacted equally to light and accommodation. There was a 4 plus enlargement of both lateral neck lobes which seemed quite soft and movable. There were no associated hard nodules. The trachea appeared to be in the midline. There were no associated glands or nodules in the neck. The heart, lungs, abdomen and extremities appeared normal.

On admission to the hospital, a repeat basal metabolic rate was reported as plus 21. Temperature was 97° F., pulse 92 and weight 146 pounds. He stated that he had originally lost 35 pounds but had since gained 25 pounds.

Laboratory data were essentially normal.

On August 16, 1949 a subtotal resection of both lateral lobes as well as the pyramidal lobe was carried out.

On the second postoperative day the patient became restless, talkative and rapidly lapsed into coma. His temperature was elevated to 104° F., and he sweated profusely. His pulse raced so fast that it was almost imperceptible.

Treatment consisted of ice packs and cold water enemas. Lugol's solution was administered by vein and by Levin tube. Chocolate milk and Karo syrup were given by Levin tube, and salt and water losses were compensated for by intravenous fluids. The patient was well sedated and placed in an oxygen tent.

On the fifth postoperative day, his temperature returned to normal, and he improved rapidly.

Pathologic report: The first specimen consisted of a large irregularly shaped piece of brownish-red tissue which measured 8 by 3.5 by 2 cm. The tissue had a rather firm consistency. On section, the cut surfaces ranged from light yellow-brown to dark red and had a uniform slightly spongy appearance throughout. In one area there was a small dark collection of what appeared to be old blood. Several representative sections were submitted for microscopic study.

The second specimen consisted of a roughly oval-shaped piece of reddish-brown tissue measuring 6.5 by 3.0 by 2.0 cm. and had a relatively smooth external surface. On section, the cut surface resembled that of the other specimen.

Microscopic examination: Sections of thyroid taken from both pieces showed an essentially similar histologic picture. The thyroid acini varied moderately in size and shape, some being distended with pink-staining colloid material, with the lining cells flattened. In others the lining cells were columnar in shape and contained little or no colloid substance. Some of these latter showed papillary enfoldings of the epithelium into the acini lumen. All variations between these two extremes were also seen. The stroma was infiltrated by lymphocytes occasionally, and in areas the fibrous tissue septa were widened

and prominent. Small areas of extravasated blood were seen and, in one or two instances, the thyroid tissue had lost its staining characteristics suggesting the presence of a small focal area of infection.

Diagnosis: Primary hyperplasia of thyroid gland showing irregular involution.

Case 3—A 69 year old white woman was first admitted to Mount Sinai Hospital in Miami, Florida on June 14, 1950. Her chief complaint was a loss of 68 pounds and extreme nervousness of one year's duration.

Physical examination revealed evidence of obvious weight loss. There was a nodular mass in the region of the thyroid and thymus gland, measuring approximately 3.5 cm. in diameter. A basal metabolic rate, two months prior to admission, was plus 95. She had been treated with propylthiouracil by her family physician, receiving 300 mg. daily. The basal metabolic rate at the time of admission to the hospital was plus 59. The condition appeared to be a toxic diffuse nodular goiter with a possibility of malignant degeneration. An electrocardiogram showed evidence of auricular fibrillation but no evidence of acute myocardial disease. The blood pressure was 165/80, and during her hospital stay the pulse rate ranged between 88 to 90 per minute. The temperature was within normal limits. The patient was placed on a 5000 calorie per day diet and given 300 mg. of propylthiouracil daily, in preparation for thyroidectomy. She remained in the hospital for six days and was then discharged with orders to continue with propylthiouracil, 300 mg. daily, and also to continue with a high calorie, high protein diet.

She was readmitted to the hospital on June 28, 1950 and at that time, her basal metabolic rate was recorded as plus 27, and she had gained 7 pounds. Within the week following her second admission she gained an additional 8 pounds. Her pulse rate was 84 per minute, and her blood pressure was 170/70. She still showed evidence of auricular fibrillation. Propylthiouracil was discontinued on July 10, 1950 and she was then given Lugol's solution, 10 drops, three times daily. The preoperative basal metabolic rate was plus 15. On July 15, 1950 a bilateral subtotal thyroidectomy was carried out under general anesthesia.

The patient's immediate postoperative condition was good. The following day, she became extremely restless and apprehensive. Her temperature was 101.2° F., and her pulse rate 100 per minute. Her respirations were 18 per minute. She was placed in an oxygen tent and given penicillin, 200,000 units, every four hours and 400 mg. of AUREOMYCIN® every six hours. On the second postoperative day, the temperature rose to 103.6° F. with a pulse of 120 per minute.

Routine emergency treatment of the thyroid storm was carried out as described in the preceding case report but to no avail. A bedside electrocardiogram showed auricular fibrillation with myocardial damage but no evidence of a myocardial infarction. The following day, the dressing was changed and the wound inspected. The incision was noted to be healing with no evidence of wound infection. A bedside chest plate was taken and showed no evidence of pulmonary consolidation or infiltration. The same afternoon, while taking medication, she suddenly became rigid, her pupils became fixed, her color cyanotic, and she quietly died.

Diagnosis: Hyperthyroidism due to toxic adenoma.

Treatment of Thyroid Storm

As Rea states,[15] the disturbing feature in the treatment of thyroid crisis or storm is that there is no specific therapy to date, and that fundamentally the cause of this condition is still obscure. It is not certain whether the primary difficulty lies in the thyroid gland itself or whether other organs, such as the adrenals, liver, pituitary, etc., are the sites of the defect. If the primary organ at fault is the thyroid gland, it is unknown whether the symptoms are due to an excess of normal secretion or to an abnormal secretion. Lahey[16] stated as his opinion that, "Most thyroid deaths are largely liver deaths." The results of a thorough review by Foss, Hunt and McMillan[4] show that neither the heart, liver, thyroid or thymus alone seems to be at fault in thyroid crisis. Threatening thyroid crisis is a condition of impending dehydration and acidosis. Until we know the

FIGURE 3. Refrigeration blanket.* Hypothermia unit (has electrical refrigeration). Equipment provides constant, dependable, convenient temperature with minimum weight.

cause of thyroid overactivity, we shall not understand crisis. However, it must be recognized early and heroic treatment must be instituted immediately. A complete therapeusis has not yet been found.

Present day management of thyroid storm is essentially symptomatic.

1. Refrigeration: It is extremely important to control the hyperthermia present. One method which seems to be highly efficacious is the use of a refrigeration blanket (figure 3). Using such a blanket was considered in the treatment of case 1, but as one was not quickly available, such treatment could not be carried out.

Hyperthermia can also be controlled by ice-water enemas and alcohol sponge baths. Increase of heat elimination is the single most important treatment up to the present time. The ideal condition for accelerating the process is to surround the patient with cold dry air so that there is a maximal temperature gradient between the patient's body and his surroundings to promote conduction, convection and radiation in a dry atmosphere conducive to evaporation.

2. Iodine: The administration of iodine reduces the output of thyroid hormone and therefore affords as rapid a means as possible for controlling thyrotoxicosis. The administration of iodine (30 drops of Lugol's solution intravenously or 10 drops in tap water by rectum) reduces the production of thyroid hormone. Sodium iodide, intravenously, allows for increased speed of action. Lugol's solution (10 drops three times daily, in chocolate milk by mouth) should also be given. Thus, Lugol's solution should be administered by vein, by mouth and by proctoclysis. Iodine would play a more important role if patients were not so resistant to the drug, because of previous treatment. Improvement may still occur after so-called "iodine fast" has developed.

3. Carbohydrates: Karo syrup and chocolate milk should be given by Levin tube to protect the hepatic glycogen reserve from the accelerated metabolism.

4. Fluids: Abundant fluids are given intravenously for fluid loss and necessary electrolytes are administered to correct dehydration. There is present a glycogen-depleted liver and marked electrolyte imbalance. Often over 6000 cc. of fluid with sodium chloride are given daily, intravenously.

5. Sedation: Profound sedation is essential. Much of the increased heat is due to thyrotoxicosis over which there is no control, but it is certainly increased by frantic muscular activity of the patient. Morphine sulfate as well as SODIUM AMYTAL® or Nembutal, intravenously, should be administered. If one prefers chloral hydrate, it may be given by Levin tube. Larger doses of these drugs are necessary than for other acutely ill patients. Irritability must be avoided to help reduce heat production and oxygen consumption.

6. Oxygen: The patient should be placed in an oxygen tent because of the acute demands of body tissue for oxygen. Probably there is more oxygen demand than in any other disease. Oxygen is given to prevent tissue anoxia, reduce heat production and oxy-

*Manufactured by Thermo-O-Rite Products Company, Buffalo, New York.

gen needs. It is well known that air hunger with rapid respiration and muscular effort increases oxygen consumption and heat production. Thyrocardiac patients tolerate oxygen deficiency poorly.

7. Chemotherapy: Prophylactic chemotherapy or antibiotics should be administered to avert any intercurrent infection.

8. Vitamins: Vitamins should be given to combat their great loss.

9. Corticotropin: The recent work of Szilagyi[17] suggests the further trial of corticotropin in thyroid storm. The suggested dosage is 20 to 30 mg. every six hours for from five to eight days, the length of the administration depending on the eosinophil count and the 17-ketosteroid output.

10. Spinal anesthesia: Rea[15] has reported a dramatic response in one case of thyroid storm using spinal anesthesia. The basis for this therapy is that spinal anesthesia temporarily de-enervates the adrenal gland.

11. Digitalis: Digitalis is administered if required. It should be remembered that thyroid patients have an increased tolerance to digitalis (134 per cent). Thyrocardiac patients should be given digitalis preoperatively.

In summary, the whole treatment of thyroid storm is symptomatic. Therapy will continue to be of a rather empiric nature until a specific cause of the condition is known.

Conclusions

1. We wish to emphasize that in spite of adequate and careful preoperative care of the toxic thyroid patient, postoperative storm may and still does occur.

2. Three recent cases of thyroid storm, following careful and adequate preoperative care, are reported.

3. The signs and symptoms of thyroid storm are reviewed.

4. The etiology of thyroid storm is discussed.

5. The treatment of thyroid storm is still expectant and supportive. Each symptom is treated separately.

6. The use of the refrigeration blanket as a possible adjunct in the treatment of thyroid crisis is suggested.

7. One may postulate or theorize that thyroid storm should be anticipated more in those instances in which initial basal metabolic rates are between plus 80 to 100, and in those instances where there is great weight loss. (In the three cases just reported the basal metabolic rates were plus 90, plus 86 and plus 95.) Although we cannot draw definite conclusions from only three cases, it is interesting to speculate that such may occur.

8. The diagnosis of thyroid storm must be made immediately because of the great toxicity created. Treatment of an heroic nature must be instituted immediately, as time is of the essence to preserve life.

We are indebted to Dr. Capone for allowing us to use case 2 in this paper and also for his advice and suggestions.

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Topical Estrogens for Chronic Acne Vulgaris

IRVING SHAPIRO

Newark, New Jersey

Acne vulgaris, its etiology and incidence, are briefly discussed. A regimen employing topically applied natural estrogens for resistant, severe types of cystic and pustular acne is described. Results obtained from this regimen proved excellent in 70 per cent of such cases, with a minimum incidence of unwanted side effects.

IRVING SHAPIRO

THAT acne vulgaris is almost a physiologic occurrence during adolescence is attested by Bloch's[1] finding that 80 per cent of students examined at age 17 had the condition in some degree. Orthodox antiseptic and peeling technics are successful in controlling approximately 85 per cent of all cases treated.

X-ray therapy has been widely employed in the treatment of resistant cases. This method, however, requires specialized training and shows a high incidence of relapse, particularly in the chronic cystic type of acne. Reporting on a series of 58 patients with acne who had been followed for 5 to 20 years following x-ray therapy, Crawford[2] listed 40 per cent as partially successful to poor results.

Since Hamilton[3] delineated the relationship between androgens or androgen/estrogen ratios and the appearance of acne, increasing prominence has been accorded to the therapeutic role of estrogens in the condition. Oral estrogens have been widely used in the treatment of acne,[4-9] but in women who have no menstrual irregularity and in men, where there can be no evidence of estrogen deficiency, it seems particularly illogical to use estrogen to influence skin metabolism by first subjecting it to systemic circulation. The more so is this true since topically applied estrogen exerts the desired effect at the desired site with a minimum incidence of side effects.

FIGURE 1. A 19 year old white girl with cystic pustular scarring acne of face and back for five years. Previous treatment with salves, lotions, vaccines, diets was unsuccessful. Severe premenstrual flare-up. General health good except for irregular menses treated by endocrinologist with oral estrogens with no effect on acne.

FIGURE 2. After 12 weeks of treatment with Premarin lotion to face only, remission is apparent. Untreated back is unchanged. Menses still irregular as was the case before beginning treatment.

Becker[10] has recently confirmed the fact that 17-ketosteroid excretion in acne patients does not vary significantly from the normal pattern and agrees with Sulzberger who has long adhered to the theory of a special local susceptibility to androgens as a decisive factor in the development of acne.

Estrogens, locally applied, can produce profound effects[11] including atrophy of the sebaceous glands[12] without systemic action while, in larger amounts, they may be absorbed through the intact skin, producing the same physiologic estrogenic influences as would follow administration by mouth or injection.

With these considerations in mind, and keeping the utilization of the atrophic influence of estrogens on sebaceous glands without systemic effects as a prime goal in the management of acne vulgaris,[3] I have for the past five years investigated the use of natural estrogens in several forms and in varying concentrations in the clinical control of this scarring and disfiguring disease of young people.[13,14]

This study is concerned with the small group of cases of chronic cystic and pustular relapsing acne. It includes degrees of involvement from recurrent mild cases to severe grades of scarring acne which had resisted all previous efforts at therapy including diets, vitamins, quartz rays, x-rays to the limit of tolerance and vaccines. The following criteria were observed to avoid including cases which might have natural spontaneous remissions:

1. Disease process of more than five years' duration and getting worse (primarily cystic and pustular types).

2. History of relapse after Alpine rays,

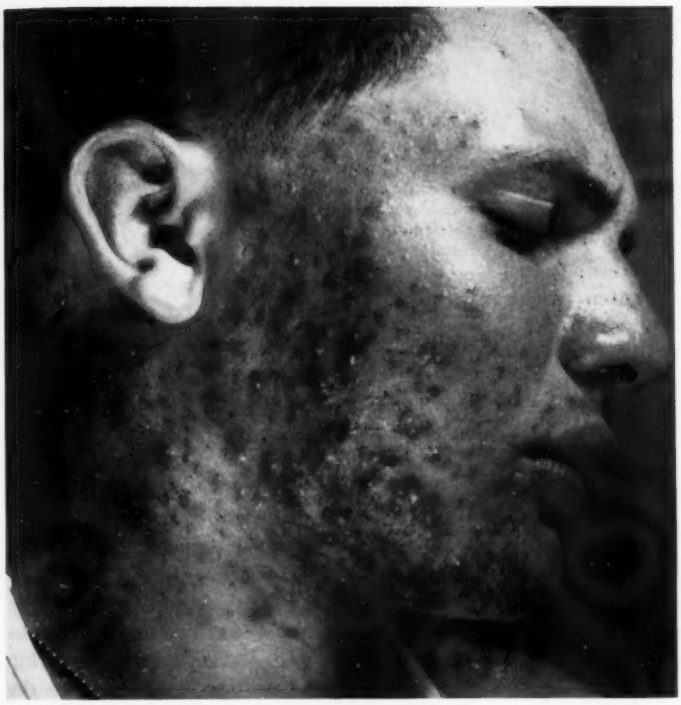

FIGURE 3. A 17 year old white student with confluent cystic and keloidal scarring acne of face, neck, chest and back of four and a half years' duration, becoming much worse nine months before treatment. Previous treatment with vaccines, diets, lotions, x-rays and penicillin had no effect.

FIGURE 4. After 16 weeks of treatment with topical estrogens the cysts have drained and severe scarring is present. The untreated chest, neck and back are unchanged. No change in breasts, libido, erections.

diets, vaccine therapy and x-rays to tolerance.

3. Patient in good general health with no apparent metabolic dysfunctions.

Method of Study

While the approach must be individualized, as with most therapeutic plans, a remission of refractory chronic severe acne may be induced in six weeks in approximately 70 per cent of cases by application to the lesions of 1.0 cc. of a special PREMARIN® lotion twice daily. This lotion contains in each cubic centimeter 1.0 mg. of conjugated estrogens (equine).*

The earliest indication of improvement is usually a sharp reduction in oiliness of the skin. Once this change has appeared the dose is tapered off sharply to a maintenance level of one daily application of 0.5 to 1.0 cc. of the lotion for an additional six to eight weeks. Unless dosage is reduced at this point there is the possibility that systemic estrogen effects may occur. Stubborn areas, however, obviously require more persistent attention.

Only 10 per cent of cases require a greater concentration to produce satisfactory initial results. Such patients are given a similar special Premarin lotion containing 2.5 mg. conjugated estrogens (equine) per cubic centimeter. Cream containing conjugated estrogens (equine) in potencies of 2.5 mg. per gram and 1.25 mg. per gram, respectively, have also been employed in treatment of acne vulgaris with good results, but the lotion is more satisfactory from the standpoint of initiating therapy. Premarin cream containing 1.25 mg. of conjugated estrogens (equine) is excellent, however, for maintenance therapy once the condition has been brought under control.

Approximately 10 per cent of patients treated according to this regimen have undergone relapse after therapy was discontinued but the relapses were mild in nature and readily controlled by a second course of treatment. While no specific dietary regimen is enforced, patients are directed to obtain adequate rest and attention is paid to the eradication of dental and other foci of infection.

In women it is common to observe premenstrual flare-ups of acne (when endogenous estrogen production is at a low level) during the first month or two of treatment. As the skin becomes drier and assumes more feminine characteristics of texture and appearance these flare-ups subside without recurrence.

Usually help is sought for acne of the face only and the fact that treatment of the face only results in improvement of that area without any change in an affected chest or back would seem to indicate a purely local effect of the topically applied estrogen. Especially is this so when the beneficial influence can be attained without disturbance of the menses in women and without altered libido or gynecomastia in men.

TABLE 1

CHRONIC ACNE VULGARIS
TOPICAL TREATMENT WITH ESTROGEN CREAM
(2.5 mg./gm. sodium estrone)

	WOMEN	MEN
Number of patients	16	10
Age	17-70	18-30
Duration of acne (years)	4-22	3-15
Total dosage (mg.) of estrogen	105-700	150-650
Duration of treatment (months)	1-7	1-6
Results:		
Excellent	10	6
Good	2	2
Fair	2	1
Therapy discontinued	1	1
Results unusable	1	

Results

Table 1 indicates results obtained with the use of a special Premarin cream containing 2.5 mg. conjugated estrogens (equine) in a series of 16 women and 10 men. Table 2 summarizes results in 36 women and table 3 shows results in 28 men, both groups having been treated with a special Premarin lotion containing 1.0 mg. conjugated estrogens (equine) per cubic centimeter.

Both sexes responded to a correctly indi-

*Dr. J. Jewell, Medical Director of Ayerst, McKenna and Harrison, Ltd., supplied special potencies of Premarin cream containing 1.0 mg. per gram and 2.5 mg. per gram and lotion containing 1.0 mg. per cubic centimeter and 2.5 mg. per cubic centimeter water soluble conjugated estrogens (equine) expressed as sodium estrone sulfate.

TABLE 2

CHRONIC ACNE VULGARIS IN WOMEN
TOPICAL TREATMENT WITH ESTROGEN LOTION
(1.0 mg./cc. sodium estrone)

Number of women	36
Age	17-40
Duration of acne (years)	5-18
Total dosage (mg.) of estrogen	60-1200
Duration of treatment (weeks)	6-16
Results:	
Excellent	25
Good	3
Retreated:	
Good	2
Fair	2
Side actions:	
Local pruritus	4
Withdrawal bleeding	1

TABLE 3

CHRONIC ACNE VULGARIS IN MEN
TOPICAL TREATMENT WITH ESTROGEN LOTION
(1.0 mg./cc. sodium estrone)

Number of men	28
Age	17-45
Duration of acne (years)	5-30
Total dosage (mg.) of estrogen	240-1400
Duration of treatment (weeks)	6-20
Results:	
Excellent	18
Good	5
Retreated:	
Good	2
Side actions:	
Pruritus	1
Gynecomastia	2

vidualized dosage of topically applied estrogen and of the total of 90 patients, 70 per cent underwent remission of severe cystic and pustular acne vulgaris which had proved refractory to all other therapeutic approaches. Only one woman (2 per cent) experienced withdrawal bleeding as a result of topically applied estrogen and only two men (5 per cent) developed gynecomastia during therapy. In view of the severity and recalcitrance of the conditions and the attendant psychologic trauma, these side effects are considered insignificant compared with the beneficial effects observed.

Summary

A brief discussion of acne vulgaris, its incidence and etiology, has been given.

A regimen employing topically applied natural estrogen for resistant severe types of cystic and pustular acne has been presented.

Results from such a regimen are excellent in 70 per cent of such cases with a minimum incidence of unwanted side effects.

Conclusions

Seventy per cent of cases of chronic scarring acne vulgaris, refractory to other forms of therapy, responded to topically applied natural estrogens. A lotion of conjugated estrogens (equine) has these advantages:

1. High local concentration of estrogen exerting a direct effect on the lesions.
2. Flexibility of dosage control.
3. No unwanted side effects with correctly adjusted dosage schedule.
4. Acceptable to both sexes, unlike creams and tinted pastes.
5. Compatible with other therapy.
6. High degree of effectiveness even in recalcitrant cases.

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The Treatment of Postmyocardial Infarction Shoulder–Hand Syndrome With Local Hydrocortisone

HERBERT BERGER*

Berger Clinic, Tottenville, New York

In a series of 18 consecutive cases of the shoulder-hand syndrome, a causalgic state which is one of the sequelae of acute myocardial infarction, favorable results were obtained by injections of hydrocortisone in trigger areas about the shoulder girdle.

A NOT inconsiderable number of patients who survive a session with coronary occlusion develop the shoulder-hand syndrome[1] in either extremity or occasionally in both arms and hands. This condition may be quite crippling and actually initiate more distress and discomfort, albeit less danger, than the predisposing myocardial infarction. This condition has been studied since it was described by Osler.[2]

It is currently believed that the syndrome of pain in the shoulder referred to the hand, accompanied by limitation of motion about the shoulder girdle and trophic changes in the hand resembling causalgia, is initiated by a train of noxious impulses arising in the damaged heart muscle. These are conducted to the upper extremity along nervous pathways in a way similar to that in angina pectoris with referred pain in the arm. Once the pattern is established, pain may persist and even increase in intensity after the source of the difficulty in the myocardium has healed. This may be due to the establishment of trigger points in the involved areas of the arm, hand and shoulder segments on a somatic basis of distribution.[3]

Many forms of therapy have been advocated and some patients respond to each. In

*Berger Clinic, Tottenville, Staten Island, New York.

personal experience with many of these troublesome situations, success has been achieved now and then by ethyl chloride spray, procaine injections of trigger areas, needling, physiotherapeutic modalities like diathermy, infrared lamps, massage and by roentgen therapy. No one form of therapy was as successful as the use of adrenal steroids in the form of ACTH or cortisone. These materials gave more uniformly good results than any of the other technics employed, although each of the others was successful in some patients.

However, there are serious objections to the use of these endocrines in a patient who has recently had a myocardial infarction. In the first place some of these patients have been in cardiac failure. It is somewhat hazardous to treat these individuals with steroids that may cause sodium storage and consequent edema, which might again precipitate cardiac decompensation. Similarly coronary artery disease frequently has been termed a contraindication to the use of cortisone or ACTH as these materials may actually precipitate arterial damage and a new occlusion. The loss of potassium engendered by the use of these potent chemicals is particularly threatening to those who already have electrolyte imbalance. Finally, a complication in the form of a new occlusion may go unnoticed because the pain threshold of the patient may be raised so high as to render him, and his physician, unaware of this serious situation.

Hydrocortisone Therapy

When the intrasynovial administration of hydrocortisone, or compound F, was first reported, this seemed an ideal way to relieve the discomfort of osteoarthritis without disagreeable systemic effects as this material, we are told, acts only locally.[4] Could this substance do as much for our postcoronary shoulder-hand syndromes we might have a medicament with all the advantages of cortisone and none of its dangers.

In a series of 18 consecutive unselected cases this hope seems to have been realized. Hydrocortisone in 50 mg. doses (chosen arbitrarily, less may do) was injected into any painful trigger area about the shoulder girdle. The injection was repeated at 48 hour intervals where necessary, that is when the pain had not disappeared or had recurred. The table summarizes the experience with this technic. As will be noted, most of the patients needed only one injection. The largest number was four. Sites of injection were all about the shoulder girdle but anterior locations exceeded posterior 18 to 2. The total number of injections exceeded the number of patients as some received multiple doses. Anterior sites included the pectoralis major and/or minor, the anterior fibers of the deltoid and possibly the intercostals. Posterior sites were the supraspinatus and the infraspinatus as well as posterior deltoid fibers. None of these patients were treated with sympathetic ganglion block or surgery of the sympathetic system.

Procaine was not used for skin anesthesia as this medicament, in itself, has been useful in the treatment of this malady. Since a needle was introduced, we have no way of knowing whether the mere puncture of the needle actually cured the patient rather than the steroid. A review of patients treated in the past, however, reveals no such spectacular series of salutary results by needling alone. Even the most enthusiastic advocates of this method, those who reintroduced the ancient Chinese art of discission, have never reported in their writings, exhibits or personal communications a 100 per cent improvement such as we have noted in the 18 cases reported.[5] In addition, some of these patients, as indicated in the table, had been treated by a variety of such technics without success, until hydrocortisone therapy was initiated.

Four of the patients treated received hydrocortisone initially. All others serve as their own controls as they had had the symptoms for some time and had been treated with some or all of the modalities noted above.

Case Report

The following case report indicates one of the gratifying results. H. B., a 67 year old white man, had a second coronary occlusion in December 1952. He recovered sufficiently by February 1953 to permit resumption of a

RESULTS OF TREATMENT

AGE	SEX	DATE OF OCCLUSION	ONSET OF S-H SYNDROME	TREATMENT						RESULTS	
				Ethyl Chloride *(No. times)*	Needling *(No. times)*	Procaine *(No. times)*	Physiotherapy *(No. times)*	Compound F		Days to Complete Relief of Pain	Days to Complete Relief of Disability
								Site of Trigger Area	No. of Injections and Dates		
56	F	1-2-53	4-8-53	5	3	8	diathermy 8	pect. minor	1 inj. 5-3-53	1	18
62	F	3-1-53	3-30-53	3	0	12	0	pect. minor	1 inj. 4-28-53	2	14
51	F	12-30-52	2-4-53	*	0	4	0	ant. deltoid	1 inj. 5-1-53	at once	21
65	M	**	4-15-53	0	0	3	0	ant. chest intercostals	1 inj. 4-29-53	1	4
46	F	3-12-53	4-20-53	0	0	0	0	ant. deltoid	1 inj. 4-27-53	1	20
72	F	2-17-53	3-22-53	8	0	12	diathermy 12	ant. chest	2 inj. 5-3-53	4	†
76	F	11-16-52	1-24-53	0	0	‡	0	ant. chest supraspinatus	4 inj. 4-22-53 4-24-53 4-26-53 4-27-53	7	28
70	F	2-16-53	3-8-53	5	1	6	massage daily	infraspinatus	1 inj.	2	12
67	M	12-22-52	3-7-53	12	2	9	diathermy 9 massage daily	pect. minor ant. deltoid	2 inj. 5-2-53 5-4-53	2	46
66	M	2-29-53	3-30-53	3	2	7	massage	supraspinatus	1 inj. 5-4-53	1	22
72	F	3-31-53	4-28-53	0	0	0	0	ant. chest	1 inj. 5-1-53	2	14
48	M	3-2-53	4-14-53	0	0	6	massage	ant. chest	1 inj. 5-7-53	1	3
57	M	3-16-53	4-23-53	0	0	7	0	deltoid	2 inj. 5-5-53	3	14
51	M	3-1-53	4-7-53	0	0	2	diathermy 2	ant. chest	1 inj. 5-1-53	1	12
54	M	3-31-53	6-1-53	0	0	4	0	pect. major	1 inj. 6-10-53	1	7
51	M	5-3-53	6-16-53	0	0	0	0	ant. chest	1 inj. 6-16-53	1	6
37	M	5-16-53	6-27-53	0	0	0	0	ant. chest	1 inj. 6-27-53	1	3
48	F	4-23-53	5-30-53	0	0	0	0	ant. chest	1 inj. 6-1-53	1	12

*Footnotes on next page.

sedentary life. He retired from business. He had low grade cardiac failure during the entire illness, requiring a mercurial diuretic about twice a week and a strict low sodium regimen (2 gm. of sodium daily). He received anticoagulants in the form of heparin until March 15, 1953.

On March 7 he first complained of pain in the shoulder and inability to use his right hand. The condition rapidly limited the movements of his right arm until he could not abduct the arm from the side more than 20 per cent. He could not reach his left shoulder with his hand nor could he move his arm behind him to reach his homolateral back trouser pocket. The hand became stiff and swollen so that he could not grasp a comb, razor or eating utensil. Actually he could not have used these implements properly as he was unable to reach his head with his right hand. He was treated with ethyl chloride repeatedly, needling, procaine in all trigger points, diathermy and massage.

The condition remained unchanged until May 2 when the steroid was first used in the pectoral muscles. Fifty milligrams were injected one inch below the coracoid process and one-fourth inch below the skin. It was at this spot and depth that he felt the most exquisite pain with the needle. The injection was quite painful, necessitating a sedative that night. The next day he had no pain and motion of the extremity had improved so that he could touch the contralateral ear. He was given 50 mg. more in the deltoid on May 4 and he progressed to full recovery on June 15 without any further medicament. He had no pain at the time of the second injection on May 4 but a tender area in the deltoid was found, after considerable searching about. This was the worst case in the series.

It must be emphasized that all of these cases were acute—of less than three months' duration. In each instance relief of pain appeared at the latest in 24 hours. Occasionally it appeared at once and the objective evidence of improvement started at the same time but the condition took some time to clear up entirely.

Summary and Conclusion

Eighteen patients with postcoronary occlusion shoulder-hand syndromes were treated with hydrocortisone locally in trigger points about the shoulder girdle. Each patient experienced some or total relief of pain in 24 hours and gradually the limitation of motion and trophic changes disappeared as well. Since many of these patients had been treated by other methods before the initiation of this therapy, it would seem that this technic may be superior to other forms of treatment. The last four patients received no other treatment.

Possibly those individuals who required several injections of hydrocortisone might have needed only one if the right trigger area had been found the first time. However, the long-standing cases may well have multiple areas needing treatment. There are many causes of the causalgic state other than myocardial infarction. We hope to use hydrocortisone in some of these later.

*Patient was instructed in use of ethyl chloride and used it several times daily.

**Exact date unknown. Patient had angina pectoris since 1949. Several severe attacks of pain in February 1953 but no serial cardiographic changes. Condition is known to occur with angina pectoris without myocardial infarction.

†Not completely relieved when last seen on 7-14-53.

‡Patient first seen 4-11-53. Had many tender areas and was treated with intravenous procaine (280 cc.) in 1 per cent solution on 10 consecutive days. No change in symptoms prior to use of hydrocortisone.

*Footnotes on next page.

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DIAGNOSTIC CLINIC

The Diagnosis of Poliomyelitis

MARTIN H. SEIFERT*

Northwestern University Medical School, Chicago

This paper is an attempt to help the practitioner organize his thinking in relation to poliomyelitis. It is the author's feeling that with the routine of thought and procedure outlined, it is entirely within the province of the general practitioner to make a diagnosis of poliomyelitis early in the course of the disease.

MARTIN H. SEIFERT

THE diagnosis of poliomyelitis may be simple and obvious or extremely difficult and obscure. The disease assumes importance entirely out of proportion to its relative rarity because of its hysteria-producing effect, its public health implications, its crippling effect, and the economic problem it produces. It is a seasonal disease usually occurring during the summer and fall months and yet during the last four years there have been but six months in which no single case passed through the communicable disease service at the Evanston Hospital.

Most cases occur between July 1 and November 1, and family life and community activity have been markedly influenced by this fact. Almost every family suspects poliomyelitis in every sick member during the warm months of the year. Therefore, it is not surprising that we see many patients now in whom the family suspected poliomyelitis for several days before the physician became convinced of the diagnosis.

The average physician is likely to see only one case every 5 or 10 years, as indicated by dividing the number of physicians by the number of cases in an area. Since about 20 per cent of cases are bulbar in nature, the average physician would expect to see only one bulbar case every 25 to 50 years in his own practice. I shall try, therefore, to tell you a few simple things, learned from 23 years of rather intimate contact with the disease, to take with you on your daily rounds.

You may argue that since we do not know a specific, definitive, curative treatment for this disease, early diagnosis can make very

*Associate in Medicine, Northwestern University Medical School; Chief of the Poliomyelitis Service, Evanston Hospital; Attending Physician, Cook County Hospital, in contagious diseases, Chicago, Illinois.

Presented before the thirty-eighth annual Assembly of the Interstate Postgraduate Medical Association at Chicago.

little difference. However, there are two facts which I believe to be true which do make early diagnosis important. These are: (1) The patient who is put at complete rest as a result of early diagnosis, or at least suspicion, of poliomyelitis is likely to have less involvement than one who is active during the early days of the disease; (2) the patient with bulbar poliomyelitis who comes under proper treatment early has a much better chance of survival than the patient who has had one or more spells of anoxia before treatment begins.

How, then, can one make an early diagnosis? Certainly the most important quality of the physician in diagnosing any disease is *suspiciousness*. I would urge that when illness with fever occurs during the summer and fall you *think* of poliomyelitis. If you consider it, you will at least try to rule it out.

Diphasic Polio

The first phase in the diphasic, or misnamed "dromedary" type is an indefinite and undiagnosable febrile period. For this reason, I feel that any child with a febrile illness during the summer and fall should be kept in and relatively quiet until his temperature has been normal for three or four days, rather than for one. Many heartaches caused by unnecessary exposure of others and by excessive activity during the early period of the disease would then be obviated. The period between the prodromal phase and the onset of the recognizable phase of invasion of the central nervous system will vary from one to five days. The patient usually feels quite well but tires more easily than usual.

A recurrence of illness, after a short period without fever, should immediately heighten suspicion that one is dealing with poliomyelitis. In some patients the central nervous system symptoms may be present from the beginning, but the diphasic pattern is probably more common. Such symptoms as backache, muscular aching and headache, especially in children, in whom headache is unusual, should markedly increase this suspicion. Usually, irritability and a fretful night or two occur early, and a mother will frequently remark that her child has been restless during the night, unable to quiet down for any considerable period.

Encephalitic Polio

In the more uncommon encephalitic type, drowsiness may come early, but irritability, fretfulness and restlessness are far more common. Apprehension on the part of the patient is commonly present and significant. Hyperesthesia sometimes manifests itself in areas over the trunk or extremities, often noted by a mother while trying to bathe a sick child. Nausea and vomiting are common; constipation is the rule. Diarrhea is rarely present, and in my opinion usually is due to a coincidental gastroenteritis. Photophobia and pain on deviation of the eyes are common: dizziness and headache which increase in the upright position are common and significant. Urinary retention is a common symptom in adults.

I would plead for hesitancy in the custom of giving sulfonamides or antibiotics at once to patients with indefinite, nonspecific febrile illnesses. Sulfonamides are harmful if the patient does prove to have poliomyelitis, and antibiotics serve only to placate the family and to salve the conscience of the physician. If you have a virus infection, "flu" or whatever you call it, antibiotics and sulfonamides are worthless anyway. These drugs themselves are producing more and more difficulty. Rather, I would recommend that if suspicion is aroused you recheck the patient in 6 to 12 hours to see if the signs are changing.

Bulbar Polio

In bulbar poliomyelitis the onset is not infrequently more abrupt. Vomiting is more commonly present. The definitive evidence of bulbar poliomyelitis is the result of involvement of the cranial nerve centers which regulate the swallowing mechanism. One of the earliest signs is a tendency to keep clearing the throat. This is merely the beginning of difficulty in swallowing the normal 1000 to 1500 cc. of salivary and mucous secretion of the upper gastrointestinal and respiratory tracts, caused by beginning weakness, paresis or paralysis in the muscles of deglutition.

More marked difficulty manifests itself in

nasal regurgitation, particularly on taking fluids. This indicates paresis or paralysis of one or both sides of the soft palate is already present, and coincidentally with this there develops a noticeable nasal, or more accurately, a palatal twang in the voice. It is not to be confused with the nasal voice of a cold or the "full head" tone of sinusitis or mononucleosis. It is, when fully developed, identical with the voice of a patient with a cleft palate.

Presence of a distinctive palatal twang or nasal regurgitation in a patient without a cleft palate is adequate evidence of bulbar poliomyelitis. We repeatedly see patients who have had these symptoms for several days without suspicion of poliomyelitis. If you see a patient regurgitate through the nose on taking fluids, if you hear a palatal twang, and you look in the patient's throat and there is no cleft palate, *that is bulbar poliomyelitis.*

Diplopia is another relatively common sign which I considered rather innocent until this year. All the patients I saw with diplopia as an early symptom just went ahead and got well, but this year I have seen one fatal case and one very severe case heralded by diplopia. Facial paralysis, usually unilateral, rarely bilateral, occurs commonly in some epidemics. Irregularity of respiration also may indicate bulbar involvement. Actual weakness of respiratory function from spinal paralysis of the respiratory muscles usually comes much later.

Examination Procedure

I want to present to you a young lady who was stricken with a strange malady while on a trip this summer. She was in Bergen, Norway, at the time and suddenly had some trouble. What kind of trouble did you have, Janet?

PATIENT: First I was sick to my stomach and then when I started swallowing, water came out of my nose. Later on my neck got stiff and I couldn't get up off the bed. Also, my talking.

DR. SEIFERT: Also something strange about your talking?

PATIENT: Yes. I couldn't make sounds like "fifty" or "wonderful."

DR. SEIFERT: Now listen to her pronounce the following words: wonderful, kitty-cat, Amsterdam, five and a half, glamour girl.

(Patient repeated these words after Dr. Seifert.)

I particularly wanted Janet to come down because, while I can imitate the voice of a total paralysis of the palate better than she can at this stage, she demonstrates, as I cannot, the tone of a *partial* palatal paralysis. I particularly wanted this patient because she is a *bulbospinal* case, with very little involvement, it is true, but she demonstrates features of both types. You can still hear an overtone in her voice. Remember that as the palate is becoming paralyzed all you will hear is that overtone in the voice.

Looking into her throat when she says "Ah" or "Uh" you can see that her palate still tents up toward the right; in other words, the left side of her palate is somewhat weaker than the right side.

The next step is to ask the patient to sit up. The patient with poliomyelitis almost always will help himself up with the arms, will turn toward one side; an infant will grasp the rungs on the crib; an adult will roll to one side or push himself up with his elbow. Janet still sits in the tripod position by preference because her back is still a little tight.

Can you kiss your knees? Almost. Probably this morning she hasn't had a warm bath yet, and maybe after that she could.

The third step is to ask the patient to drink water. Janet still has some trouble, and as a result she swallows cautiously. A child four years old learns to swallow as she is swallowing now in just one bad attempt. If she takes swallow after swallow as you or I would, she will have nasal regurgitation or she will choke. When you give a child a glass of water to drink and he takes one swallow, waits a while and then takes another, look out for trouble.

The fourth step is a general medical examination to look for signs of other infection.

The fifth step is to try the Brudzinski maneuver. In doing this, be sure the patient is lying flat, then with one hand on the front of the chest and the other on the back of the head, roll the head gently from side to side. Then bring the head forward to the limit of flexion in that patient. Put firm pressure on

the back of the head at the end of flexion and see whether the knees come up. The Brudzinski test will never be positive unless pressure is used after the limit of voluntary flexion of the neck is reached.

I think one of the failures that we commonly have in examination of patients is failure to get a positive Brudzinski sign. Often we have to teach the intern or resident what to do. I always make some silly remark like, "Now, Janet, just let me have your head. I'll give it back to you after this is over." It makes the patient smile or laugh and relax, and you can make them let go much more easily. When you bring the head forward you must bring it to the limit of flexion, and then you must put extra steady, firm, not jerky, pressure on the back of it. If you do not put extra pressure on the back of the head after you have brought it to the limit of flexion, you will never see a positive Brudzinski sign.

Janet, will you bring that leg out on top of the cover? If you really watch her, you will see abduction, external rotation, flexion of the hip, flexion of the knee, even motion of the ankle; you will see extension of the knee, extension of the hip, adduction and internal rotation. You don't need to do much more to examine the legs for reasonably normal function. We don't want a detailed muscle analysis on an acutely ill patient when we are examining for diagnostic purposes.

The sixth step is straight leg raising. With one hand over the knee and the other under the heel, gently raise the leg and determine at what angle the hamstrings begin to tighten. I find this more useful than the Kernig maneuver because I need to measure with my eye only *one angle* and that is the hip. If this angle is recorded from time to time, it serves as a quantitative aid for determining whether tightness is increasing. If the angle is 80 degrees in the morning and in the afternoon it is only 60 degrees, that is a significant difference and may mean a good deal in diagnosis.

The seventh step is the head drop. Never warn the patient what you are going to do; just put your hands under the shoulders and pick them up gently. This young lady does not have a head drop any more. This is a pretty good illustration of the fact that the head drop has nothing to do with weakness or paralysis of the anterior neck muscles, because she still has weak anterior neck muscles. I can push her head down with very little pressure, and yet she no longer has a head drop. Normally, when a patient starts to sit up you will immediately see the V of the tensing sternocleidomastoids with the head coming up with or preceding the trunk.

The eighth step is to test the cranial nerves. I would like you to sit up while we do this, Janet. Will you raise your eyebrows like this? Pinch your eyes shut tightly; make a face like a skunk eating bumblebees. Now, follow my finger with your eyes. Remember that diplopia (which is not present here) may frequently occur in just one quadrant; this is not at all unusual. I have a patient right now with paralysis of just the right rectus muscle.

Wrinkle your nose, Janet. Show your teeth —widely; now whistle. You will notice that this young lady still has weakness on one side of her face, and it shows in her best when she puckers her lips to whistle. Now, Janet, blow up your cheeks. She cannot hold air because one side relaxes. You should also ask your patient to stick out his tongue as straight as he can, and to bite down hard.

On looking into this patient's throat we find deviation of the median raphe of the palate. Deviation of the uvula, which hangs loose, is not so significant; watch the median raphe. Deviation of the tongue is not present, and she has a good gag at this point. The patient may lose the gag reflex, however.

The ninth step is to test the reflexes. In my opinion a fairly heavy, well-balanced hammer is much better than a light conventional triangle. A problem arises where reinforcement is necessary, where the simple Jendrassik maneuver perhaps does not work. There is a simple thing which often helps in getting the knee jerks. Will you try gently, Janet, to straighten your legs? Not so hard, just gently. If the Jendrassik maneuver does not work, have the patient use the quadriceps group which is going to respond to a patellar tendon stimulation, and then the patient cannot inhibit that muscle group from working.

For examination of the superficial tendon reflexes I have never found any instrument equal to a wooden splinter from a broken tongue blade. Slight bilateral differences are frequently considered important. It seems to me that consistent and gross variations are the only significant findings. Also important are reflexes that are exaggerated early, fade after a day or two, then gradually return.

Testing for areas of hyperesthesia or a level of anesthesia is the tenth step. If the latter is present, it is more likely that a spinal cord tumor or a transverse myelitis is responsible.

In testing muscle power, the eleventh step, I have already mentioned the fact that you can observe the motion of the legs as the patient brings them out onto the covers without help—do not move the covers all the way off the leg, but just partially so that the patient has to lift his leg around and over.

Here is a simple method for examining the power of the upper extremities. Have the patient fix the arm at an angle of about 20 degrees from the side of the chest, with the elbow at a right angle. Now don't let me move it, Janet. As I perform various motions you will notice that I can push the deltoid right down, so it is not normal. Try to extend the elbow, to flex the elbow. Try pronation, supination, internal rotation of the shoulder, external rotation of the shoulder. Then we try the grip, and that is about enough for a sick patient.

Remember, if a patient is acutely ill, detailed muscle analysis is both useless and harmful; and let us avoid *multiple examinations*. Careful observation of the patient's movements during the course of the examination may be sufficient to tell about gross weakness. There are simple ways of testing major muscle groups in each extremity in a few seconds with little exertion by the patient.

The twelfth step is to observe the patient's ability to breathe. If he talks in short phrases his vital capacity is small. Feel for the strength of the expanding chest. Palpate the intercostal muscles for tenderness. Having the patient count as far as he can with a single breath is a practical quantitative measure of his respiratory power.

Step number 13 is to palpate the skeletal muscle groups for tenderness.

Other Diagnostic Procedures

Remember always that in either poliomyelitis or meningitis occurring in infancy, spinal rigidity may occur very late, and convulsive seizures, muscle twitching, bulging fontanels, or fever without discernible cause may be the first signs of central nervous system infection.

It may be well to mention here also that localized tremors or twitching sometimes occur in poliomyelitis and, in my experience, have usually foretold rather severe muscular involvement of these areas. Another caution should be that when localized tremors or twitching occur they may well be due to brain tumor or abscess, aneurysmal hemorrhage, or other intracranial pathology.

If, on examination or history, adequate suspicion of central nervous system involvement is elicited, a lumbar puncture should be done. In a case with frank bulbar signs puncture is unnecessary and perhaps even dangerous, if for no other reason than that it may excite the patient and produce crying with excessive secretion of mucus and increased difficulty in swallowing. In a case with obvious scattered or spotty paresis or paralysis, the diagnosis is obvious and puncture is unnecessary because it has no purpose other than to aid diagnosis. In a case with uniform symmetric paresis or paralysis, puncture should be done to eliminate the possibility of radiculitis (Guillain-Barré syndrome). In a nonparalytic or preparalytic case, differentiation from other infections of the central nervous system requires puncture and careful examination of the spinal fluid.

As a routine, I would wish to know the cell count and the type of cells present; the concentration of total protein, of glucose and of chlorides. The pressure of the spinal fluid may be significant. In poliomyelitis or encephalitis it is usually normal or slightly increased. In meningitis it is likely to be considerably higher. In poliomyelitis, cultures of the fluid are sterile.

In cases of space-occupying lesions, such as tumors, the pressure is likely to be very high, but it is also likely to be reduced to normal

after the removal of very small amounts (3 to 6 cc.) of fluid. In poliomyelitis the fluid is likely to be clear or slightly opalescent. Subarachnoid hemorrhage produces frankly bloody fluid from beginning to end of the tap. Meningitis usually produces an opalescent, milky or frankly purulent fluid. The cell count, to be accurate, should be done before the fluid is 30 minutes old, as the few cells frequently found in poliomyelitis may disintegrate in a very short time.

Usual cell counts in poliomyelitis fluid are mildly to moderately increased and range from 10 to 300. Rarely, I have seen fluids show counts of 1000 to 1500, and on one occasion I saw a paralytic poliomyelitis with 2500 cells, almost entirely polymorphonuclear. In my experience exceedingly high counts have frequently been accompanied by severe paralysis but this has apparently not been universally the case. If the puncture is done during the first 48 hours of illness, the differential count is likely to show a predominance of polymorphonuclear forms. After 48 to 72 hours, the usual finding is about 50 per cent polymorphonuclear and 50 per cent mononuclear. After 72 to 96 hours the usual poliomyelitis fluid will show 80 to 100 per cent mononuclear forms.

It is possible to have normal spinal fluid findings at the time of the original puncture even in paralytic poliomyelitis. This has occurred in a small percentage of the 1800 cases seen by the Evanston Hospital group in the past 23 years. Recently, Dr. Josephine Earlywine of our staff reported an incidence of 20 per cent of normal fluids in patients under three years of age, with some weakness or paralysis in all of the patients showing normal counts. Dr. Edith Nicholls of Danville, Pennsylvania, reported 13.8 per cent of 320 patients with normal spinal fluid findings.

Proteins are usually normal or slightly increased early in the course of poliomyelitis. After four days the proteins usually rise moderately.

Glucose is usually normal (two-thirds blood level) in poliomyelitis and in most viral infections, with a tendency to be elevated a little in the encephalitides. Bacterial infections reduce spinal fluid sugar. Chlorides are normal except during the early stage of tuberculous meningitis, when there is a marked tendency to a decrease in the chloride level.

Differential Diagnosis

The differential diagnosis of disease commonly confused with poliomyelitis includes a multitude of conditions. The most common disease coming to my service in the past 10 years mistakenly diagnosed as poliomyelitis by myself and others has been infectious mononucleosis. A fair percentage of these patients will have some signs of central nervous system involvement. Headache, stiffness of back and neck and, in several cases, a positive Brudzinski sign and head drop have confused the picture.

Clinically, the occurrence of marked swelling of the nasopharyngeal lymphoid tissue with a "full head" voice, the presence of posterior cervical, occipital or preauricular lymphadenitis, enlargement of the spleen, or tenderness of the liver with obvious tonsillitis or pharyngitis should make one suspicious of glandular fever. Negative spinal fluid findings, and atypical mononuclear cells in the blood smears, complete the picture.

Most important in differential diagnosis are the meningitides. Here as a rule the patient is more toxic. Rigidity is more pronounced. Opisthotonos is more common. Meningitides are more common in winter and spring; poliomyelitis in the summer and fall. Petechiae may appear and indicate meningococcal septicemia. Leukocytosis characterizes the blood picture while blood and urine tend to be normal in early poliomyelitis. The spinal fluid in the purulent meningitides will usually show marked clouding, marked polymorphonuclear pleocytosis, sharp decrease in sugar, and the presence of the causative organism in smears and cultures. Tuberculous meningitis tends to show increase in mononuclear cells and proteins with decrease in sugar and chlorides. Lymphocytic choriomeningitis is proved only by animal inoculation.

One must at times differentiate epidemic or equine encephalitis. Much more common, in our experience, have been the encephalitides

occurring in the course of or, as in mumps, before the onset of other virus diseases. Mumps meningo-encephalitis, measles encephalitis and influenzal encephalitis have been most common. Their prevalence in the community or signs of their existence in the patient are the criteria for suspicion.

Mumps meningo-encephalitis tends to complete recovery without sequelae. Measles and influenzal encephalitis are much more serious in both mortality and sequelae. Chickenpox and German measles also produce serious encephalitis but fortunately this occurs only rarely. Encephalitis may also occur following smallpox or rabies virus vaccine, and here the history of the use of such preparations is obvious evidence. Tetanus may be a problem but a history of injury without protection by toxoid or antitoxin, fibrillary muscle twitching, hypertonia of masseter muscles and other groups with a normal spinal fluid, are usual. Meningism accompanying febrile diseases is distinguished by finding the evidence of these diseases.

Several cases of radiculitis (Guillain-Barré syndrome) have occurred in our series, where the albuminocytologic dissociation in the spinal fluid is the distinguishing feature. Cell count is normal, but proteins reach levels in the 300 to 1000 mg. range. Suspicion of this condition should always arise when weakness is symmetric.

Brain tumors and abscesses should be suspected when focal signs occur. One hint of a space-occupying lesion has already been mentioned—the decrease of spinal fluid pressure with the removal of small amounts of fluid. Transverse myelitis should be suspected when the involvement is symmetric and a sharp level of anesthesia or hyperesthesia is found.

Rabies may be confusing and the history of animal injury is important. Scurvy-produced subperiosteal hemorrhage, with tenderness and limitation of motion of the thighs, was commonly seen in the North Carolina epidemic of 1944. About once each year we see a case of typhoid fever sent in as poliomyelitis, with increasing headache and fever. Negative spinal fluid, leukopenia, sustained fever, bacteremia, and cultures of stools and urine usually make the diagnosis quite definite.

Injuries, particularly about the hip and lower back, may confuse the picture, and transient synovitis of the hip or epiphysitis may be confusing. Subarachnoid hemorrhage is an occasional problem but the grossly bloody fluid and frequent history of injury or previous episodes differentiate this condition. Hysteria with or without paralysis has been seen on rare occasions. I would warn against this diagnosis as I have seen great harm come from it. Hysteria, in my experience, does not produce fever.

Coxsackie virus infections have been included in the differential diagnosis largely because the first isolations of Coxsackie viruses were made from poliomyelitis patients. However, the actual manifestation of infection with group A Coxsackie virus is probably herpangina. The principal manifestation of group B Coxsackie viruses is epidemic pleurodynia, and is not actually concerned in differential diagnosis.

Acute porphyria with diffuse bilateral paresis or paralysis, similar to that seen in the Guillain-Barré syndrome, was seen on my service for the first time this year. Here, exposure of urine (obtained early in the acute phase) to sunlight causes it to turn a dark, port-wine color, and the Watson-Schwartz test for urinary porphobilinogen should be positive. A history of previous abdominal crises and red urine with perhaps a similar family history is also suggestive.

I had a harrowing experience this year in which, as nearly as I can reconstruct the sequence of events, a cellulitis developed in the muscle and perispinal tissues of such virulence as to produce a perimeningitis, with the meninges so severely irritated by the adjacent inflammation as to produce severe headache and spinal rigidity with a spinal fluid count of 1500 cells (90 per cent polymorphonuclear). In this case the sugar was normal, ruling out bacterial infection, and the sterile cultures supported this impression. I urge you to consider poliomyelitis when signs of nondescript infections occur, especially in summer, and to keep the patient at rest until the diagnosis can be established.

DIAGNOSTIC CLINIC

The Treatment of Portal Hypertension

ALTON OCHSNER*

Ochsner Clinic, New Orleans

Portal hypertension, which may be intrahepatic or extrahepatic, is a serious disease. Intrahepatic portal obstruction is usually due to cirrhosis. In portal hypertension, varices between portal and systemic circulations develop. Varices in the lower end of the esophagus are most important, because of the danger of ulceration and massive hemorrhage. Severe hemorrhage in the patient is dangerous because of fatal exsanguination and also because of the possibility of development of liver necrosis subsequent to anoxia during the period of hypotension.

Although temporary expedient procedures may be used to control bleeding from esophageal varices, the only definite procedure is operation which shunts the blood from the portal system into the systemic venous system.

UNTIL relatively recently portal hypertension was a condition for which we could do comparatively little. Due primarily to the investigations of Whipple and Blakemore, the prognosis in portal hypertension is no longer as poor as it has been previously.

ALTON OCHSNER

We have a patient to present now and I am grateful for her appearance here. Mrs. F. is 49 years old. In 1949, she noticed for the first time that she had swelling of her abdomen. She was seen in the outpatient department of Mercy Hospital (Chicago) where she had previously been a patient on several occasions. A diagnosis of cirrhosis of the liver with ascites had been made.

She has been tapped 26 times, and one time, according to her record, 15,000 cc. of fluid was removed. What the total amount removed was I do not know.

On one occasion she had massive hemorrhage. She has had an esophagram which I have been told, although I have not seen the film, showed esophageal varices.

Fortunately, due to the treatment that she has had, namely, correct diet and tapping to relieve pressure, she has improved remarkably. She has had no paracenteses since June 1953, and she now feels very much better.

In the meantime, Mrs. F. has developed an umbilical hernia and two inguinal hernias. These, of course, are due to the tremendous increases in pressure within the abdomen and are secondary to her disease.

Unfortunately, not all such patients respond to the therapy as well as Mrs. F. Contrary to what I was taught as a medical student, cirrhosis of the liver today, as a result of the work being done by hepatologists, does not

*Director of the Section on General Surgery, Ochsner Clinic; William Henderson Professor of Surgery and Director of the Department, Tulane University of Louisiana School of Medicine, New Orleans, Louisiana.

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offer the prognosis that it did previously.

There is some controversy regarding the cause of cirrhosis of the liver. I am not a hepatologist, but I have been told by my colleagues who are interested in this problem that although alcohol has been blamed and is responsible in many instances, it is probably not the alcohol per se which is responsible for the development of the cirrhosis, but that it is the dietary deficiency which frequently is associated with the excessive intake of alcohol. We do see many patients with cirrhosis who have never imbibed any alcohol. In such instances the condition is due usually to one of two things: a dietary deficiency alone or a previous hepatitis.

I should like to present, more or less didactically, a résumé of our concept of the treatment of portal hypertension.

There are two principal groups of causes of portal hypertension, extrahepatic and the intrahepatic obstructions. There may be a congenital stenosis of the portal vein or a thrombosis of the portal vein or its tributaries. These portal obstructions occur outside the liver and include the so-called Banti's syndrome. Banti's syndrome is one in which there is a portal hypertension, but in which the obstruction is limited pretty much to the splenic vein. It is for this condition that splenectomy effects a cure. Banti's syndrome has an entirely different prognosis from that of portal hypertension associated with cirrhosis. Banti's syndrome generally occurs in younger persons and, whereas they may bleed, the bleeding is seldom as severe and the mortality rate is lower than in individuals who have esophageal varices and hemorrhage from cirrhosis.

When intrahepatic obstruction occurs, it is usually produced by cirrhosis, the obstruction being limited to the liver itself. Also, there is a portal hypertension in right heart failure, but it is of no significance here.

As a result of obstruction in the portal bed, varicosities develop between the portal and systemic circulations, in particular areas—the so-called caput medusae around the umbilicus, the hemorrhoidal veins, the communications between the gastric veins and the parietes, and the dilatation of the veins of Sappey (figure 1). The important ones, however, are those veins that become dilated in the lower end of the esophagus, with the development of esophageal varices. Although varices occur in other parts of the communications between the portal and the systemic circulations, the other varicosities are of relatively little significance. The esophageal varices, however, are of considerable significance because of the danger of massive, and far too frequently fatal, hemorrhage. Wangensteen and others believe that esophageal varices are dangerous and bleed so massively because of the digestion of the esophageal mucosa overlying these varices. This occurs as a result of regurgitation of the acid gastric chyme into the lower end of the esophagus. Because of this, Wangensteen has suggested that one way to treat this condition is to cut down the acidity of the stomach by doing either a massive gas-

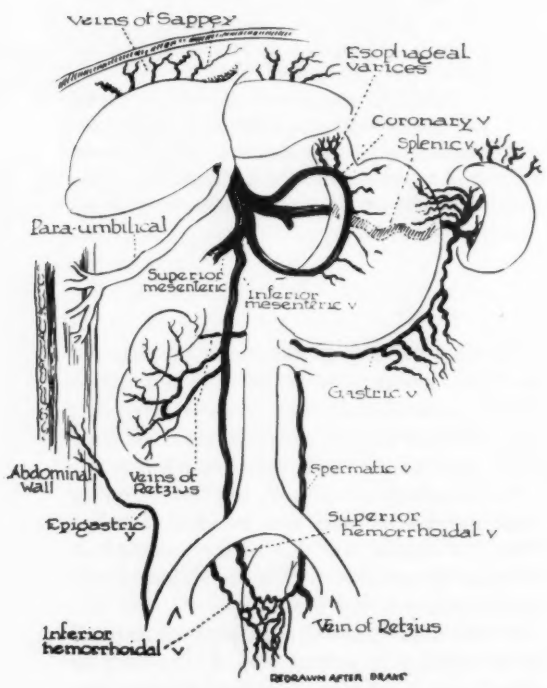

FIGURE 1. Sites at which varicosities may develop between the portal and systemic circulations.

trectomy or an esophagogastrectomy.

The varices in the portal system and the severe bleeding are of importance, as I mentioned. Fifteen per cent of patients die by the time they have their fourth hemorrhage. It has been stated that half of the patients who have massive hemorrhages from esophageal varices will die within a year from the time of their massive hemorrhage. This illustrates the danger of this complication which should not be underestimated.

There is also the danger that hemorrhage from esophageal varices will occur as a result of the hepatic necrosis which follows the marked fall in blood pressure. If this drop in blood pressure is not corrected soon enough and adequately, it will cause hepatic necrosis and the patient will die of liver failure. He may not die of shock or hemorrhage directly, but he will die subsequently if these effects are not adequately treated.

Figure 2 is a diagrammatic concept of what one sees during surgery or postmortem examination of patients with portal hypertension. There are usually three groups of veins which are enormously dilated. They are limited almost entirely to the distal third of the esophagus, but they do extend down into the stomach.

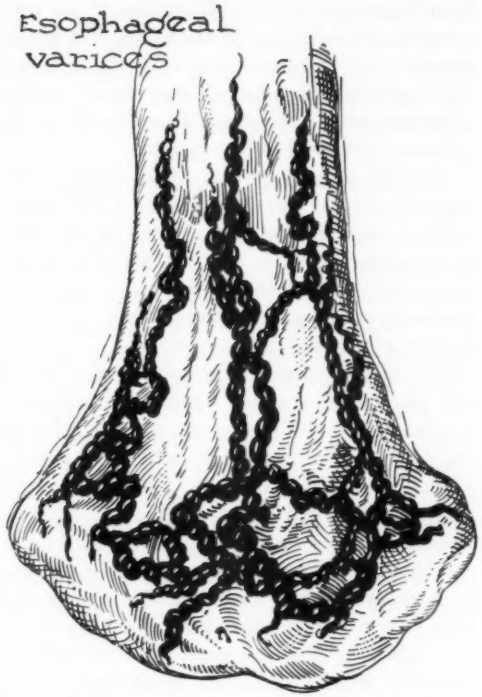

FIGURE 2. Diagrammatic concept of what is seen during surgery or postmortem examination of patient with portal hypertension.

Another condition which is associated with portal hypertension is hypersplenism. Hypersplenism is, in itself, a serious manifestation because it is associated with anemia, leukopenia and thrombocytopenia. Thrombocytopenia also predisposes to hemorrhage, so a vicious cycle is set up as a result of this condition. Not only do patients bleed from the varices but they have a greater tendency toward bleeding because of blood changes.

The other condition which the patient here, Mrs. F., shows particularly is ascites associated with hypoproteinemia. The hypoproteinemia is due to the loss of a great deal of protein-rich fluid into the abdominal cavity. If that fluid is removed, obviously it is irretrievably lost, so that the hypoproteinemia is very important. One of the reasons patients have difficulty in getting well is that their livers have difficulty repairing themselves, even with adequate therapy, because of the hypoproteinemia. The salt and water metabolism is altered and there is some evidence of an excess of an antidiuretic hormone, which tends to prevent a normal elimination of fluid.

The diagnosis of portal hypertension is not difficult to make. It is usually quite obvious. There is a history of dietary indiscretion, alcoholism or previous hepatitis. There is obvious evidence of abdominal and rectal varices. Careful and multiple liver tests indicate whether there is evidence of cirrhosis or liver damage.

Esophagoscopy is an important way of determining the presence or absence of esophageal varices, because it indirectly enables visualization of the varicosities by means of a contrast medium. Many people fear esophagoscopy because of the danger of injury to the dilated veins. I can assure you, however, that if it is done carefully there is no danger at all.

Esophagoscopy is valuable in that it not only provides visualization of the veins, but it also permits one to obtain venous pressures, and one can then determine whether there is portal hypertension. Of course, varices indicate the presence of portal hypertension.

Finally, portography is of importance because it tells where the obstruction is. Previously we resorted to portography at the time of operation when it was not actually necessary, but it is desirable to know prior to operation whether the patient has an intrahepatic or extrahepatic obstruction.

The operation which is done varies, but if one plans to do a shunt—either portacaval or a splenorenal—it is necessary or desirable to know whether or not the portal vein is patent. The operation is usually done through a thoraco-abdominal incision. This is a massive incision, and it is disquieting to explore a thorax or an abdomen preparatory to doing a portacaval shunt and find that the portal vein is completely obstructed. You go in on the right side and you can't do anything but close the wound and do a splenorenal shunt on the left side. By using percutaneous portography, injecting the contrast substance directly into the spleen and taking a roentgenogram immediately afterward, one gets excellent visualization of the portal system. One can then determine whether the block is intrahepatic or extrahepatic and in that way plan what to do.

FIGURE 3. Roentgenogram of a patient with esophageal varices.

FIGURE 4. The typical "moth-eaten" appearance of esophageal varices.

A roentgenogram of a patient with esophageal varices is shown in figure 3. The typical esophageal varices can be seen in figure 4. This is of diagnostic importance. Figure 5 is another example of extensive varices, while figure 6 shows the same patient after the varicosities have been reduced by a shunt.

The treatment of portal hypertension varies a great deal. Not all patients need surgery but every patient with portal hypertension and every patient with esophageal varices is a potential fatality. A patient who has had a massive hemorrhage requires treatment to prevent the recurrence of the hemorrhage.

There are a number of ways to treat portal hypertension. One method is resection of the stenotic area and end-to-end anastomosis of the portal vein for those relatively rare congenital lesions in which there is a congenital stricture of the portal vein. This is a curative procedure.

A palliative procedure, and one which has had quite a great deal of popularity until

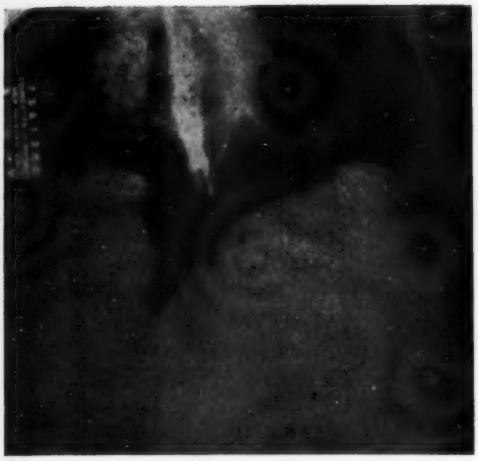

FIGURE 5. An example of extensive varices.

relatively recently, is an attempt to reduce the flow in the portal system by ligation of the hepatic artery or its radicles. As you know, Dr. Behrman and Dr. Reinhoff suggested this procedure and it has been used in a number of instances. I have never been able to see the value of this procedure, because it seems to me that any procedure that cuts down the arterial blood flow to a viscus which is already diseased is likely to interfere with the normal reparative process. Obviously, one cannot cut off all the blood supply to the liver, because if one did there would be hepatic necrosis. When a hepatic artery ligation is done, the liver does not become necrotic because there is sufficient collateral circulation to prevent severe anemia. I am quite sure that at the present time there is much less enthusiasm for this operation (which it seems to me on a theoretical basis is not sound) than there was before. Many patients have massive hemorrhages and are too sick to stand any procedure except one which carries relatively little trauma. Although these are palliative procedures, they are expedient and can and should be used.

The simplest therapeutic procedure is to attempt to prevent hemorrhage by tamponade, by means of a double balloon (figure 7). This is a very valuable and expedient procedure but it is palliative. Although the patient is relieved as long as the tampon is in place, unfortunately, bleeding frequently recurs and, therefore, the tampon cannot be used for a long period of time.

A method of therapy which has been largely abandoned (it was used as a definitive procedure, and it is certainly not that) is the injection of sclerosing agents. It is a very valuable emergency measure to tide the patient over the period during which he might bleed. During esophagoscopy the esophagoscopist can inject a sclerosing agent into the dilated varicosities and effectively clot the blood and thus prevent bleeding for a period of time.

Occasionally, in an individual who is in very bad shape and who could not stand a shunt operation, ligation of the left gastric artery and coronary veins is a lifesaving procedure. The ligation does not involve much risk, the trauma is not great, and it can be done relatively safely.

FIGURE 6. Same patient as shown in figure 5 after the varicosities have been reduced by a shunt.

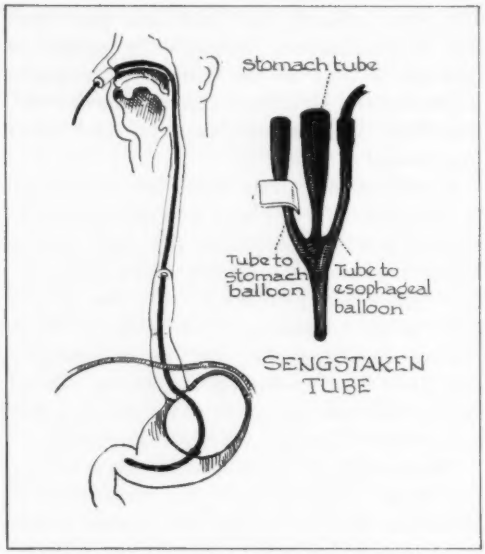

FIGURE 7. Therapeutic procedure for portal hypertension to prevent hemorrhage by means of a double balloon.

Another method, which can be used if the patient is not too sick, is multiple suture of the varices. Dr. George Crile, Jr. has advocated this procedure and has popularized it. I don't think that this is a definitive procedure; it is a good emergency method to tide the patient over until something definitive can be done. I would warn against its being used, however, for the patient who has a severe hypoproteinemia. We lost one of our patients after doing this procedure, simply because the patient did not have enough plasma proteins to heal his esophagus; his wound never healed and he died of empyema.

Still another palliative procedure is resection. I have already alluded to this. I mentioned esophagogastrectomy to remove the varicose-vein-bearing area and to cut down some of the acidity.

Finally, there is total gastrectomy, as originally suggested by Wangensteen, in order to get rid of the acid which is responsible for the ulceration.

The diagrammatic drawing in figure 8 shows the method of ligating the varices. A running catgut suture is used to incorporate the varices in the suture. This is a very good palliative operation, but it is not curative.

The only curative treatment for portal hypertension is to decrease the pressure within the portal vein. The only way to accomplish this is to shunt the blood from the portal system into the systemic system. As a result of the investigations of Whipple and Blakemore, this shunting of the blood can be accomplished in one of several ways: by a portacaval anastomosis, by splenorenal anastomosis, or, if the spleen is out—as is so often the case—by making an anastomosis with another of the portal tributaries, usually a mesenteric vein with the cava. I prefer a portacaval shunt because I think it provides a better anastomosis. I have had fewer poor results with portacaval shunts because I think they provide better anastomoses. I have had fewer poor results with portacaval shunts than with splenorenal shunts. With a splenorenal shunt there is greater danger of the shunt closing than with a portacaval shunt.

The splenorenal shunt is done without removing the kidney, as was originally suggested (figure 9). On the left side, the spleen is removed and the end of the splenic vein is anastomosed to the side of the renal vein, leaving the kidney intact. In this way the blood is shunted out of the portal system into the systemic circulation.

With the portacaval shunt there is not much limit to the size of the anastomosis (figure 10). There are some who have advocated an end-to-side shunt, dividing the portal vein as it enters the liver and anastomosing the end of the portal vein with the side of the cava. I prefer a side-to-side anastomosis because of the hope that later, after the patient has been treated for his or her cirrhosis, ultimately the blood flow through the portal system and through the liver will be re-established. In such instances we would like to have the portal vein function. A satisfactory shunt may be secured with a side-to-side anastomosis, but this still does not preclude the possibility of any blood passing through the liver later.

In conclusion, I would like to re-emphasize that portal hypertension is a dangerous disease. It is dangerous not because of the portal

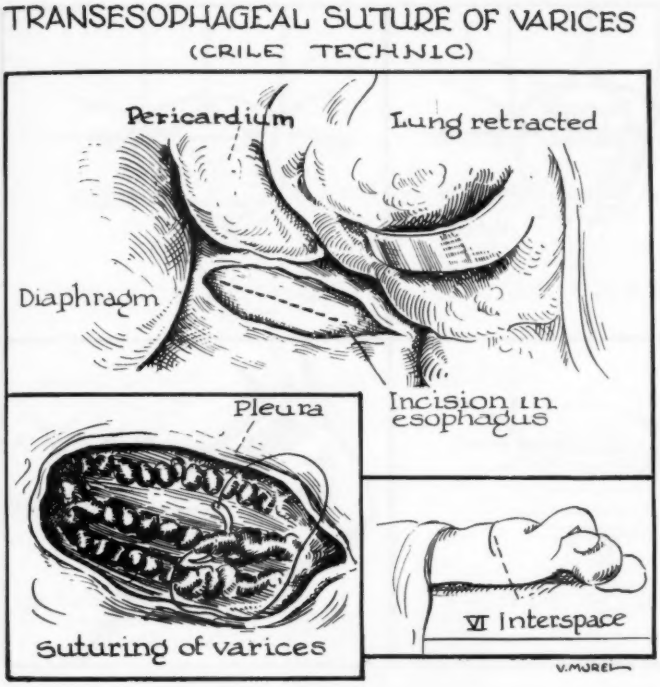

FIGURE 8. Method of ligating the varices.

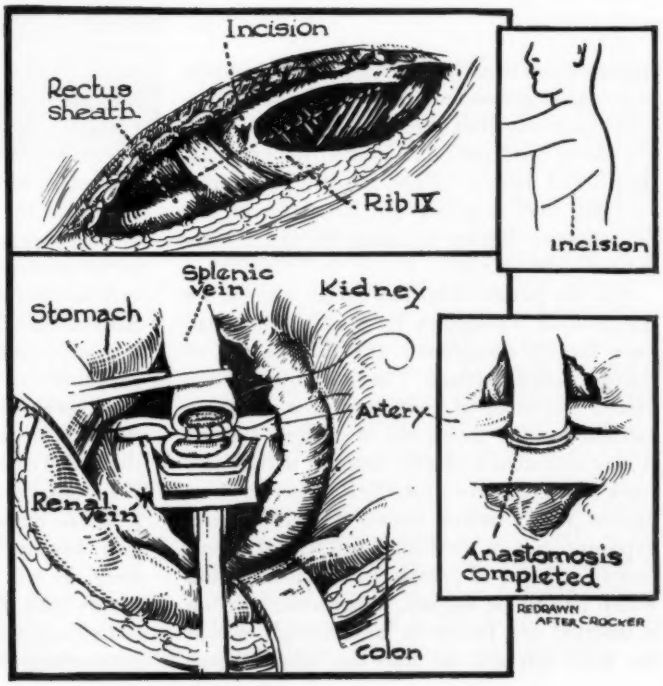

FIGURE 9. Splenorenal shunt procedure for the treatment of portal hypertension.

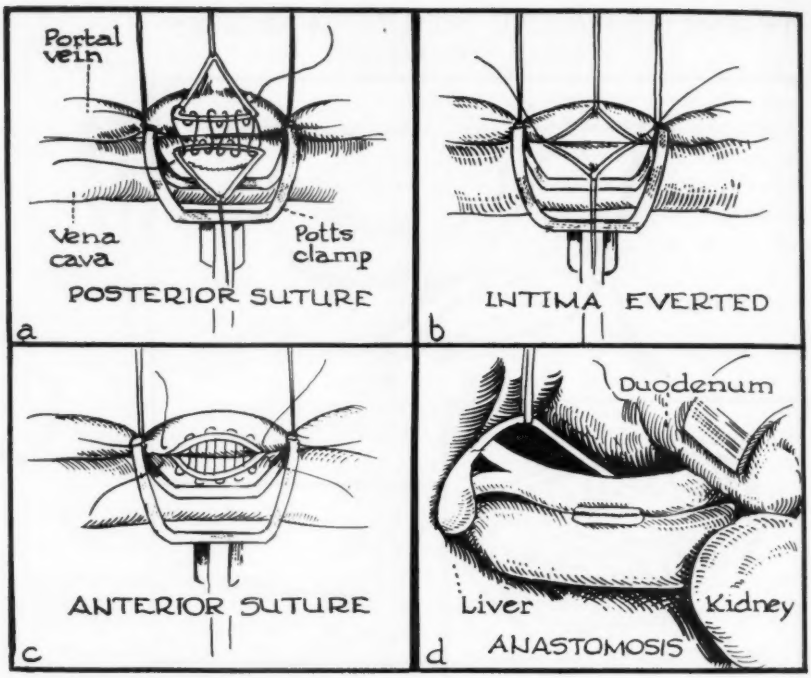

FIGURE 10. Portacaval shunt procedure for the treatment of portal hypertension.

hypertension itself but because of the sequelae and complications and, of these, the most dangerous is hemorrhage from esophageal varices. People do die from other causes; for example, they die of hepatic failure, but if a person can be tided over long enough, if he can be put on a proper dietary regimen, he can usually get well and survive.

For the patient who has severe ascites, we use another emergency treatment which had been largely abandoned, that is, the use of the peritoneal button. The button was suggested a number of years ago as a definitive method for the treatment of ascites. I think it was abandoned chiefly because it does not work as a definitive procedure. However, in a patient with massive ascites associated with hypoproteinemia resulting from loss of an excessive amount of protein in the ascitic fluid which has to be tapped, a peritoneal button is inserted and functions long enough so that the fluid can get out into the subcutaneous tissue. (As you know, this button goes from the peritoneal cavity into the subcutaneous tissue.) The proteins in the ascitic fluid can be reabsorbed; the hypoproteinemia will be corrected, facilitating the regeneration of the liver, and the vicious cycle can be broken.

These procedures, which have been used in the past as definitive treatment, should and can be used as temporary procedures to help patients over their critical periods. After the hypoproteinemia is corrected, liver repair progresses normally. So it is with the patient with severe varices who has massive hemorrhage. The liver may survive, but if the patient dies of hemorrhage in the meantime, or if he develops hepatic necrosis as a result of a severe hypotension in the systemic circulation because of inadequate blood replacement, he will not live long enough for repair of his liver to occur. Every case should be individualized, but the one thing to fear is hemorrhage from esophageal varices.

DIAGNOSTIC CLINIC

Jejunal Ulcer

SAMUEL F. MARSHALL*

Lahey Clinic, Boston

Jejunal (recurrent) ulcer may occur after any operation in which the small bowel is attached to the stomach. The discussion covers the factors influencing the development of jejunal ulcer, its symptoms and preferred management, as well as its incidence following various types of surgery for duodenal and gastric ulcer.

SAMUEL F. MARSHALL

JEJUNAL ulcer (sometimes called marginal ulcer, recurrent ulcer or gastrojejunal ulcer) may occur after any type of operation in which the small bowel is attached to the stomach, whether the procedure is a gastroenterostomy, a resection, or vagotomy plus gastroenterostomy. In view of all the vagotomies and gastroenterostomies that have been done over the past few years, it is a little alarming to realize that in the future we may see a great many more jejunal ulcers. Too short a period of time has elapsed to draw conclusions about the effectiveness of vagotomy plus gastroenterostomy.

Many factors influence the development of a jejunal or recurrent ulcer. I hope to emphasize some of the factors that can be controlled because, after all, jejunal ulcer is a man-made disease—it follows surgery. One important thing to remember is that many of the operative procedures suggested for the surgical treatment of duodenal and gastric ulcer have been developed because some of the former operations have not been successful in preventing recurrent ulceration, and because the incidence of jejunal ulcer is higher each year.

At the Lahey Clinic the youngest individual with jejunal ulcer was 22 years old and the oldest 75. The average age is about 49 years. The sex distribution is about the same as for duodenal ulcer, about 11 times more frequent in men than in women.

Most jejunal ulcers occurred in patients who had had duodenal ulcers, rarely in those who had had gastric ulcers. I have rarely seen a case of recurrent ulcer following an adequate resection of a gastric ulcer, but it can occur if the resection is not adequate.

*Surgeon, Lahey Clinic, New England Baptist Hospital and New England Deaconess Hospital, Boston, Massachusetts.

Presented before the thirty-eighth annual Assembly of the Interstate Postgraduate Medical Association at Chicago.

The shortest period between the primary operation and the onset of jejunal ulcer symptoms was two weeks. The longest interval was 32 years, and the average was six years. Allen and Welch pointed out that about a third of the recurrences in their series took place in the first year, and another third in the second year after resection. In our experience, about 60 per cent of the recurrences took place in the first three years. That is the dangerous period.

We know that more jejunal ulcers occur after a gastrojejunostomy than after a resection. We are not sure about the exact percentages because many statistics are based on history and follow-up letters and are not too reliable.

In 1942, Kiefer at the Lahey Clinic reviewed a series of cases in which resection had been performed. He found an incidence of recurrent ulcer after adequate resection of 6.4 per cent. This finding was proved by operation in one-half of these cases, and based on roentgenologic examination and clinical history in the other half.

We rarely see a jejunal ulcer after resection for a gastric ulcer. In another group of cases that we studied and presented at the meeting of the Southern Surgical Association in 1952, 411 resections for gastric ulcer were performed with no case of recurrent ulcer.

Some studies have indicated that jejunal ulcer occurs very uncommonly after gastrojejunostomy for gastric ulcer, but I do not believe this is true. One English paper reported that the incidence of recurrence after gastroenterostomy for gastric ulcer was 10.4 per cent. We would not do such an operation today because of the possibility of carcinoma. To eradicate carcinoma, a resection must be performed.

However, jejunal ulcers occur more commonly after operations for duodenal ulcers, particularly in young individuals who have hyperacidity and hypersecretion.

From our experience and that reported in the literature, it appears that the incidence of jejunal ulcer is about 15 to 20 per cent. Lewisohn, in 1924, reported an incidence in cases (not histories) studied, of 34 per cent, which is high. Willkie reported an incidence of 3.4 per cent, and Balfour at the Mayo Clinic reported in 1934 an incidence of 2.8 per cent. It is the consensus today of most men interested in gastric surgery that the average incidence of jejunal ulcer after resection is about 15 to 20 per cent. However, we believe that with adequate resection the incidence can be much less.

We now use resection for duodenal ulcer in almost all cases. Resection is performed in all cases of gastric ulcer because we cannot be certain whether the ulcer is benign or malignant. It should be remembered that a high percentage of gastric ulcers are malignant. Of the group of 411 patients submitted to surgery at the Lahey Clinic, 16.2 per cent had carcinoma. I do not believe that we can say that the ulcers had become malignant; it is a question of distinguishing between a benign ulcer and a malignant one. The only way this can be done is to hospitalize the patient and if the ulcer does not heal, to perform a resection. That is the only way to avoid missing a gastric ulcer that is definitely malignant and that probably was malignant from the beginning.

Shields Warren, pathologist for the New England Deaconess and New England Baptist Hospitals, has said that in the material obtained from patients at the Lahey Clinic he has had only four instances of gastric carcinoma that he could be sure developed from benign gastric ulcers. Even so, the pathologic evidence is equivocal and conclusions cannot be drawn from it.

The incidence of recurrent ulcer following resection is about 2 or 3 per cent in my experience. As mentioned previously, Kiefer in 1942 found it to be 6.4 per cent, but only 3.2 per cent were proved by operation.

I have studied a series of patients seen over a period of 14 years. A diagnosis of recurrent ulcer or marginal ulcer was made and some type of definitive operation was performed in 258 cases. At operation, 172 of the 258 patients had demonstrable ulcers and 86 had only deformity of the gastrojejunostomy.

Such a deformity or malfunction ordinarily indicates that an ulcer had been present pre-

viously and had healed. Eustermann and Kirklin pointed out that in a series of 62 cases they found that malfunction meant the presence of an ulcer or jejunitis or obstruction, and obstruction was indicative of a previous gastrojejunal ulcer. In many of our cases of obstruction we found that a duodenal ulcer had become active again and had reproduced the symptoms.

Case Report

The patient here is a man, 63 years old. He had a perforated ulcer in 1939. In his history he states that he had had abdominal pain as long as he can remember, 15 years before the perforation. The pain was characteristic of duodenal ulcer and was relieved by taking food. Then perforation occurred and a closure was made. He had an interval of freedom from pain, but it recurred two or three years after the perforation. In 1945 an inadequate resection of the stomach was performed.

The patient's jejunal ulcer was not apparent on a recent roentgenogram, but such an ulcer is difficult to demonstrate. Along the greater curvature there was a slightly denser area of barium that could indicate a pocketing of barium, which is frequently all that can be seen in these cases. Even though the resection was inadequate, the patient had gone for eight years, from 1945 to 1953, without any difficulty.

His first symptom was hemorrhage. He passed reddish-brown blood in the stools, which is characteristic of jejunal ulcer. Prior to that bleeding he had had no pain whatever.

This patient has never stopped smoking. (I would urge that all patients be told to stop smoking after an operation such as this, for cigarettes may be a cause of recurrent ulcer. After a patient is well established on a diet and his symptoms are well controlled, he can take a little liquor occasionally, but if he wants to take hard liquor, it should be whiskey with soda or water, not mixed drinks.) This patient has not taken hard liquor, but occasionally beer. He has not paid any attention to his diet; he has eaten everything and has had no difficulty. The unusual feature was that he had no symptoms whatever until he had the hemorrhage, and then he was nearly exsanguinated.

As illustrated by this case, in any individual who has a history of previous gastric operation, hemorrhage is good evidence that a recurrent or jejunal ulcer is present. This case was unusual in that the hemorrhage was so severe that the patient was apparently exsanguinated. The hemoglobin was 28 per cent and the patient was white, weak and frightened. His pulse was very rapid. Usually hemorrhage with jejunal ulcer is not a serious phenomenon. An emergency operation is rarely necessary for these patients, because usually they do not have massive bleeding. Ordinarily, operation is an elective procedure.

Symptoms and Etiology

In our group of 172 patients who were proved at operation to have definite ulcers, 43 per cent had hemorrhage as the first symptom. Gordon-Taylor reported hemorrhage in 50 per cent of his cases. Hemorrhage occurs much more commonly with jejunal ulcer than with duodenal or gastric ulcer. However, Wilkinson, in a study at the Lahey Clinic involving 140 cases of duodenal ulcer, reported that in 70 cases, massive hemorrhage was the first symptom. This is a high incidence of hemorrhage in patients with duodenal ulcer. If a patient has two or more massive hemorrhages he should be operated on to avoid further difficulty.

In our experience, about 20 per cent of patients with duodenal ulcer have had massive hemorrhage, whereas 43 per cent of those with jejunal ulcers have had hemorrhage.

The other symptoms of recurrent (jejunal) ulcer are characteristic. We do not know the etiologic factors in the production of recurrent ulcer, but they are probably similar to those of duodenal ulcer. Jejunal ulcers occur in the presence of high acid. In the case presented, the free acid with histamine was 22 after the resection, which is high for a patient with a resected stomach; the total acid was over 40.

Another cause of jejunal ulcer is insufficient resection. Jejunal ulcers rarely occur after operations for gastric ulcer. However, they

occur more commonly when the antrum has not been removed, in other words, after the Finsterer operation. (We have not done this operation for a number of years.)

Frequently with jejunal ulcers, evidences of obstruction develop when the antrum is not removed. The incidence of recurrent ulcer is high when the antrum has been allowed to remain *in situ*. In our experience, the recurrence rate was 54 per cent in cases where the antrum was not removed. According to Ransom, the recurrence rate is 30 to 40 per cent. If the antrum cannot be removed at the first operation, a high resection should be performed and later the antrum can be resected.

I am not too enthusiastic about the use of vagotomy, but if the ulcer involves the second part of the duodenum and is firmly adherent to the common bile duct, I believe a simple posterior gastroenterostomy plus vagotomy should be done.

I have already mentioned the importance of the occurrence of jejunal ulcers following operations for duodenal ulcers. If the stomach is transected and the surgeon is committed to resection and finds that the duodenal ulcer is irremovable, one of two things can be done: (1) the antrum can be left in place and removed at a later date, or (2) the common bile duct can be exposed, a catheter inserted into it and the resection performed safely. The antrum must be removed or the patient will have a recurrent ulcer.

It has been said that if a long loop anastomosis is made, that is, if the loop proximal to the stomach is long, the likelihood of recurrence of ulcer is increased. I do not believe that is true. It is not necessary to do posterior anastomoses. Anterior anastomoses can be done much more easily than posterior anastomoses. Furthermore, a certain number of recurrences will take place and re-operation is an easier technical procedure after anterior anastomosis. Ordinarily if the omentum is removed, an anterior anastomosis can be performed with just as short a loop as for a posterior anastomosis, and the surgeon is not limited in performing a high resection by trying to make an anastomosis through the mesocolon. We place the proximal loop at the greater curvature and carry out a high transection of the stomach. When the operation is completed, the gastrojejunal anastomosis lies transversely and the proximal loop does not become dilated. We rarely see recurrent ulcers after this type of operation and we do not encounter the dumping syndrome. It may occur momentarily after operation, but a little attention to diet and regulation of the habits of the individual patient will prevent it. Thus, the technical features are of great importance in preventing the development of recurrent ulcer after operation.

Other important features must be considered. An operation for an ulcer is a serious procedure. I do not refer to the mortality or the morbidity, but to future digestive activity. We should make the patient realize that it is a serious venture, that he cannot smoke, drink, or abuse himself with food or other measures as he might wish. If the patient is allowed to do so, he may develop a jejunal or recurrent ulcer, which is a much worse condition than that for which the primary operation was done. It is extremely important that we impress on our patients the necessity for taking good care of themselves after operation. I do not agree with individuals who say that after a vagotomy and gastroenterostomy, the patient can do as he pleases. Many such patients return with recurrent ulcer after these procedures have been done.

I would like to say just a few words about choice of treatment. When a jejunal ulcer occurs after gastroenterostomy, we always perform a resection. The Committee on Surgical Procedures of the American Gastroenterological Society stated that, from their statistics, the results following resection for jejunal ulcer were far superior to those following vagotomy. Crile reported that of 27 patients in whom the ulcer was not disturbed or the stomach altered in any way and vagotomy only was done, good results were obtained in 23 cases and poor results in 4 cases. That is a 15 per cent incidence of poor results, which is high.

We use vagotomy in the patient who has had an adequate resection but who has a recurrent ulcer. However, we perform a trans-

abdominal vagotomy because we want to see the ulcer. We also want to determine whether there is any obstruction in the jejunum, although this can usually be demonstrated on the roentgenogram, and, most important, we want to see whether the antrum has been retained. If the antrum is still present, it should be removed, vagotomy performed, and nothing else done. In some cases we have proceeded with further resection in addition to vagotomy. If resection was inadequate, we perform a high resection, leaving a very small remnant of the stomach, carry out a vagotomy, and always look for the antrum.

Summary

We rely chiefly on resection of the stomach. We employ vagotomy for those patients who have had an adequate resection, who have recurrent or jejunal ulcer, and in whom the antrum has been removed. We also use vagotomy for those patients who have not had an adequate resection; we look for the antrum, resect the stomach, and do a vagotomy. We employ further resection for those patients who have a gastrojejunal ulcer after anastomosis of the small bowel or gastroenterostomy. Vagotomy is carried out on those patients who are operated on primarily for massive hemorrhage, but resection also is performed.

Jejunal ulcer is a serious problem and one in which we can do a great deal by controlling the patient after operation and by watching out for pitfalls in the technical procedure.

BOOKS RECEIVED

New books received are acknowledged each month. As space permits, books of principal interest to our readers will be reviewed more extensively. Reviews and additional listings will be found in this issue starting on page A-72.

A Primer of Congestive Heart Failure. By George E. Burch, M.D., Henderson Professor of Medicine, Tulane University School of Medicine, New Orleans. 126 pages, illustrated. 1954, Charles C Thomas, Springfield, Illinois. $4.00.

Pneumonia. By Hobart A. Reimann, M.D., Visiting Professor of Medicine, The American University of Beirut, Lebanon. 236 pages with 19 illustrations. 1954, Charles C Thomas, Springfield, Illinois. $5.75.

Newer Concepts of the Causes and Treatment of Diabetes Mellitus; Proceedings of the Symposium on Diabetes sponsored by the New York Diabetes Association and held at Memorial Hospital and The New York Academy of Sciences, New York City, October 8, 1953. 1954, The National Vitamin Foundation, Incorporated, New York. $2.50.

A Manual of Tropical Medicine. By Thomas T. Mackie, M.D., Chairman, The American Foundation for Tropical Medicine, George W. Hunter, III, Ph.D., Chief, Section of Parasitology-Entomology, Fourth Army Area Medical Laboratory, Brooke Army Medical Center, Fort Sam Houston, Texas and C. Brooke Worth, M.D., Field Staff Member, Division of Medicine and Public Health, The Rockefeller Foundation, New York City. Ed. 2. 907 pages with 304 illustrations. 1954, W. B. Saunders Company, Philadelphia. $12.00.

Illustrated Review of Fracture Treatment. By Frederick Lee Liebolt, M.D., Attending Surgeon in Charge of Orthopedics, the New York Hospital, New York. 229 pages with 605 illustrations. 1954, Lange Medical Publications, Los Altos, California. $4.00.

Surgical Urology; A Handbook of Operative Surgery. By R. H. Flocks, M.D., Professor and Head, Department of Urology and David Culp, M.D., Assistant Professor of Urology, State University of Iowa College of Medicine, Iowa City. 392 pages with 118 illustrations. 1954, The Year Book Publishers, Inc., Chicago. $9.75.

Neurosurgery of Infancy and Childhood. By Franc D. Ingraham, M.D., Associate Professor of Surgery and Donald D. Matson, M.D., Assistant Professor of Surgery, Harvard Medical School, Cambridge, Massachusetts. 456 pages with 482 illustrations. 1954, Charles C Thomas, Springfield, Illinois. $15.00.

The Meaning of Social Medicine. By Iago Galdston, M.D., Secretary, Medical Information Bureau, The New York Academy of Medicine, New York City. 137 pages. 1954, Harvard University Press, Cambridge, Massachusetts. $2.75.

Hypertension and Nephritis. By Arthur M. Fishberg, M.D., Director of Medicine, Beth Israel Hospital, New York City. Ed. 5. 986 pages with 49 illustrations. 1954, Lea & Febiger, Philadelphia. $12.50.

Carcinoma of the Colon. By Leland S. McKittrick, M.D., Clinical Professor of Surgery, Harvard Medical School, Cambridge, Massachusetts and Frank C. Wheelock, Jr., M.D., Assistant in Surgery, Massachusetts General Hospital, Boston. 94 pages, illustrated. 1954, Charles C Thomas, Springfield, Illinois. $3.25.

DIAGNOSTIC CLINIC

Differential Diagnosis of Tumors of the Neck

CONRAD J. BAUMGARTNER*

College of Medical Evangelists, Los Angeles

Biopsy is often necessary to diagnose correctly a lump in the neck. Certain tumors, however, have characteristics by which they may be recognized. Midline tumors are rarely due to lymph node involvement. Lateral tumors may be single, either primary or secondary. Lymph node pathology is common and may be either neoplastic or inflammatory.

CONRAD J. BAUMGARTNER

It is frequently impossible to make a differential diagnosis of a tumor of the neck without the benefit of a biopsy. There are, however, certain tumors which have characteristics peculiar to themselves by which they may be fairly accurately identified.

There are more pathologic entities within the confines of the neck than in any other part of the body. In this discussion I shall attempt to outline only the important distinguishing features in a rather brief manner.

Let us then arbitrarily place these tumors into two groups: (1) tumors found in the anterior midline portion of the neck and (2) tumors located more to either side of the neck.

*Associate Professor of Surgery, College of Medical Evangelists, Los Angeles, California.

Presented before the thirty-eighth annual Assembly of the Interstate Postgraduate Medical Association at Chicago.

Anterior Midline Tumors

Lymphadenopathies limited to the anterior midline group usually do not present any diagnostic problem, as there are few lymph nodes in this region, and when they are enlarged, the causative focus can usually readily be found within the oral cavity or lips.

Actually most of the anterior midline tumors are in some manner directly or indirectly related to the thyroid gland. In this anterior midline group we shall place the following:

1. Nodular goiters
2. Thyroglossal duct cysts
3. Dermoid cysts
4. Lipomas
5. Parathyroid adenomas

Nodular goiters—We shall not discuss diffuse toxic or nontoxic goiters, as these are not tumors. Nodular goiters may definitely be classified as new growths and do not offer a diagnostic problem. Even a layman would recognize it as a large nodular goiter, and it is quite apparent that it is probably malignant.

The woman shown in figure 1 offers a little more of a problem. She has a huge swelling, filling the left anterior portion and middle of the neck, but it moves on swallowing, as is characteristic of a nodular goiter.

In the case illustrated in figure 2, there is nothing very obvious to the casual observer or examiner. Ordinary palpation may miss the pathology here.

What then is the proper method of palpating the thyroid gland? The thumb of each hand is placed directly over the trachea. The index and middle fingers are then carried deep behind the sternomastoid muscles with slight pressure toward the thumbs. The patient's head is flexed slightly and she is asked to swallow. As the patient swallows (figure 2), a rather large nodular goiter can be discovered in the right lower pole of the thyroid. This method will likewise assist in revealing a substernal goiter by the impulse from below as the patient swallows.

Thyroglossal duct cysts—Thyroglossal cysts are congenital in origin, arising from persistent embryonic thyroglossal ducts. These entities are superseded in frequency only by goiters and tumors of lymphatic origin.

A thyroglossal cyst may occur at any level in the neck, from the foramen cecum to the suprasternal notch. The majority, however, occur just below the hyoid bone (figure 3). The most common symptom is a painless swelling in the midline of the neck. Because the cyst may drain by way of the foramen cecum, there may be a history of periodic regression in size and, for the same reason, a periodic inflammation may take place. A characteristic peculiar to these cysts is that they *move on swallowing* and their contents comprise a tenacious and ropy mucoid material which is encountered in no other lesion of the neck.

Dermoid cysts—Dermoid cysts occur in the

FIGURE 1. The tumor fills the entire front and left side of the neck. Movement on swallowing designates this as a nodular goiter.

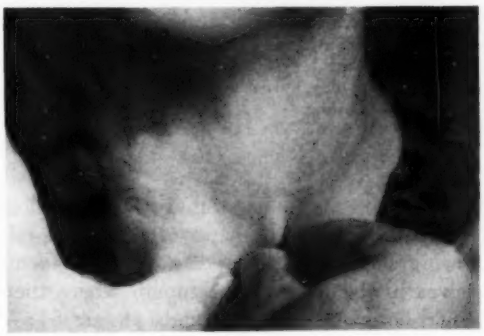

FIGURE 2. The nodule in the lower pole of the right lobe of the thyroid gland could easily be missed on superficial inspection and palpation, but is quite obvious when palpated as illustrated.

FIGURE 3. Thyroglossal cysts occur most frequently just below the hyoid bone. Content is mucoid and ropy. These cysts are unilocular and move on swallowing.

FIGURE 4. Dermoid cyst below chin. Content is of a cheeselike and doughy consistency. There is no movement on swallowing.

midline and may be confused with thyroglossal cysts. They do not, however, move on swallowing (figure 4). They may present themselves in the floor of the mouth where they could be mistaken for a ranula (figure 5). A ranula, however, is a thin, bluish, walled cyst, while a dermoid cyst has a characteristic white appearance. The contents of these cysts are the cheesy material of the dermoid. Those occurring below the chin do not move on swallowing and they are of a doughy consistency.

Lipomas—Lipomas in the neck occur most often in the posterior triangle. Next most frequently affected is the area beneath the chin (figure 6), where lipomas may be mistaken for thyroglossal duct cysts. They do not move on swallowing and aspiration will not reveal any content. It may be difficult or impossible to differentiate a lipoma from a dermoid cyst, although the latter has a more doughy consistency.

Parathyroid adenomas—Although this condition is rarely encountered, it is my conviction that it is often overlooked. One is particularly impressed by the fact that a fairly large number have been discovered at the Massachusetts General Hospital and the Mayo Clinic, while the average hospital in the United States has none, or at most only a few, listed in their files. This is no doubt due to the bizarre clinical picture of certain types of hyperparathyroidism. The disease is due to an overproduction of parathyroid hormone,

FIGURE 5. Dermoid cyst beneath tongue. This type of cyst should not be confused with a ranula. Dermoid cysts are white and doughy, while ranulas are clear, soft and blue in color, never white.

FIGURE 6. Lipoma under chin. This is the second most common location for lipoma of the neck. Lipomas are not doughy and do not move on swallowing.

caused either by a tumor or by hyperplasia of the parathyroid glands. The hormone is a regulator of calcium and phosphorus metabolism. An excess of the hormone causes an elevation of the blood calcium at the expense of bone and, conversely, a depression of the blood phosphorus; in other words, the very opposite of parathyroid tetany occurs.

What then is the clinical picture of hyperparathyroidism? I believe this is best illustrated by a caricature (figure 7). Notice the woman on the right in the figure. (Hyperparathyroidism is more common in women.) The thermometers on the wall show an elevation of serum calcium and a drop in serum phosphorus. This is due to the demineralization of bone as shown by the x-ray picture hanging on the wall. The demineralization leads to bone cysts and osteitis fibrosa cystica, with deformed bones and pathologic fractures. Therefore, the woman is deformed and has a leg in a cast. Such people often have only a vague weakness, malaise and nausea with loss of appetite. This woman shows signs of nausea and malaise; in fact she could vomit at any time. The increase in blood calcium leads to kidney stones and nephritis. The woman is also holding on to her left kidney area. The table in front of her and the night pot beneath are very significant. These patients have polyuria and the night pot floweth over. Most significant, however, is the single bone in the plate on the table, while three bones appear in the night pot. The patients have a calcium imbalance—the intake of calcium is less than that excreted in the urine. The study of calcium intake and output is the most important diagnostic procedure, and when a discrete tumor is palpable at the upper or lower pole of the thyroid in the presence of chemical findings, one should suspect a parathyroid adenoma.

FIGURE 7. Parathyroid adenoma. Clinical picture is portrayed in caricature.

Lateral Tumors of the Neck

Lateral tumors of the neck are difficult diagnostic problems because of the vast number of lymph nodes in this area and the variety of diseases which affect them.

I prefer to subdivide lateral neck tumors into two classes: (1) single lateral tumors and (2) cervical lymphadenopathies.

Single Lateral Tumors

In the group arbitrarily called single lateral tumors we may include the following:

1. Branchial cysts
2. Carotid body tumors
3. "Aberrant thyroid"
4. Single metastatic nodules
5. Cystic hygromas
6. Salivary gland tumors
7. Dermoid cysts
8. Lipomas
9. Neurofibromas
10. Hemangiomas
11. Lymphangiomas

Branchial cysts—There are two schools of thought as to the origin of branchial cysts and fistulas. One group maintains that they are the result of an inclusion of a branchial cleft, particularly the second. The other group maintains that they are of thymic origin, similar to embryonic thyroglossal duct cysts. Without definitely taking sides, I would like to point out that branchial cysts, and particularly fistulas, roughly follow the pattern of embryonic thymic ducts.

Both branchial fistulas and embryonic thymic ducts come from the lateral wall of the pharynx and pass beneath the midportion of the posterior belly of the digastric muscle, then over the carotid and beneath the anterior fibers of the sternomastoid. The fistulas frequently, however, pass between the external and internal carotid arteries before passing superficial to the common carotid.

Branchial cysts (figures 8 and 9) are always unilocular and are located beneath the investing fascia—over the carotid sheath and under the anterior fibers of the sternomastoid muscle. They are almost always in this relationship and may occur at any level. Most cysts are found in the upper third of the neck, while the fistulas appear in the lower neck (figure 10). The proportion, incidentally, of cysts to fistulas is 10 to 1. The cysts are nontranslucent and may be very tense, resembling a solid tumor. They are not soft and flabby as are cystic hygromas, are rarely bilateral (figure 11), and do not move on swallowing. The contents are variable, depending on infection; they are often of a milky, watery nature, but are never viscid like the contents of thyroglossal cysts.

The cystic contents may contain cholesterol crystals (figure 12) which must be searched for in the freshly aspirated specimen. These crystals are readily identified, as they have somewhat the shape of the State of Utah.

The cysts may become inflamed and, therefore, tender. Malignancy was not found by Pemberton in a single instance of 291 cases reported by him, but Hendricks and Ward have reported several very definite cases which were without a doubt examples of malignant transformation of branchial cysts.

Carotid body tumors—This is fortunately a rare condition. Warren of the Lahey Clinic reported 24 cases which were operated on at the clinic up to 1953. Carotid body tumors are slow-growing, asymptomatic, solid, circumscribed lesions, situated in the crotch formed by the bifurcation of the common carotid artery, which is at a level with the upper border of the thyroid cartilage.

There is considerable disagreement as to the relative malignancy of these tumors.

FIGURE 8. Branchial cysts occur most frequently in the upper third of the neck. They are in definite relationship to anterior and deep fibers of the sternomastoid muscle.

FIGURE 9. Branchial cysts are always unilocular and do not transmit light.

FIGURE 10. Branchial fistula. Opening is in relationship to anterior fibers of sternomastoid muscle.

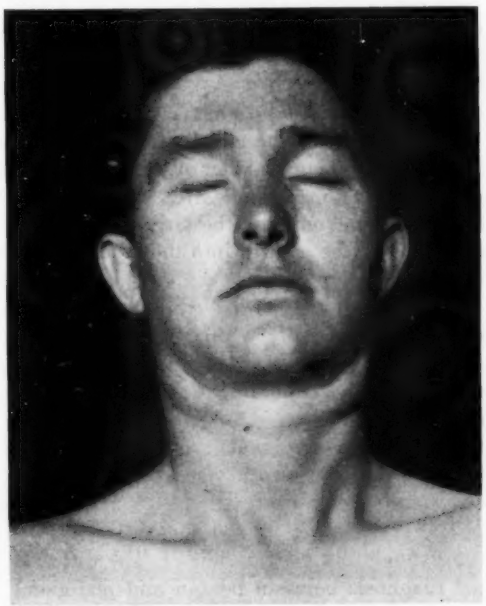

FIGURE 11. Branchial cysts are rarely bilateral. Note again the location and relationship to sternomastoid muscle.

Lahey maintained that few are actually malignant, while Harrington, Clagett and Dockerty of the Mayo Clinic believe at least *half* are malignant.

Carotid body tumors are definitely deeper than the branchial cysts with which they are most easily confused. They may bulge into the pharynx. There is pulsation from the carotid vessels, which also may elicit a bruit. Because of their position these tumors may be moved laterally, but not up and down.

I have stated that fortunately these tumors rarely occur. This statement is made because of the potential danger of surgery. Removal of such tumors may be hazardous because of the danger of thrombosis of the carotids from manipulation, and chiefly because cerebral damage is common when ligation of the common external and internal carotids becomes necessary during the tedious dissection. At the Lahey Clinic the mortality rate was 50 per cent in six patients for whom such ligation was necessary. The deaths were due to cerebral complications. At the Mayo Clinic, the common and internal carotid arteries were ligated 14 times in a total of 33 carotid body tumors. There were five deaths, all preceded by hemiplegia, a mortality rate of 30 per cent. I stress this in the differential diagnosis, as the physician should inform himself and his

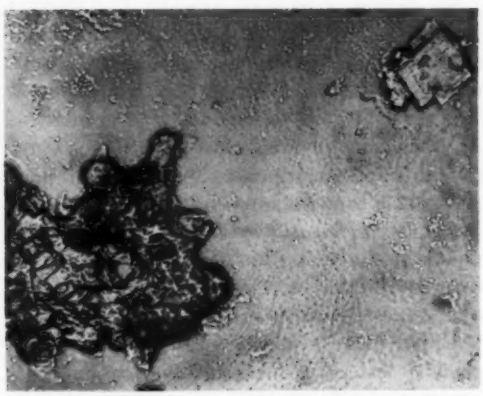

FIGURE 12. Cholesterol crystals in aspirated contents of branchial cyst. The crystal is easily identified by its notch, giving it the shape of the State of Utah.

patient before searching for what might be a carotid body tumor. Certainly a mortality rate of 30 to 50 per cent, in the best of clinics, is too high a price to pay for a condition which may well be benign.

Not long ago I attended a hospital staff meeting at which was presented a case report of an excision of a carotid body tumor in a 20 year old nurse. It became necessary to ligate both common external and internal carotids. The surgeon reported that the patient had a smooth convalescence with only temporary hemiplegia. The tumor was benign! I wonder how many of you would be at ease if your own 20 year old daughter had a so-called *temporary* hemiplegia because of a benign tumor which was symptomless!

Aberrant thyroid—The term "aberrant thyroid" should be deleted from our terminology. There was a time when this was considered to be misplaced embryonic thyroid tissue, only occasionally malignant. It is my firm conviction that each and every one is metastatic from a primary lesion in the thyroid gland, and that minute section-for-section examination of the entire thyroid gland will reveal a primary tumor, however small, in each case.

An aberrant nodule may be single, but actually more than one node is often involved, and the jugular vein group at any level is commonly affected. Therefore, the so-called aberrant thyroid tumor may be mistaken for a carotid body tumor.

When any nodule is present, the thyroid should be palpated to determine a possible connection. When one approaches these nodules during surgical dissection, suspicion of "aberrant thyroid" is aroused by the increase in vascularity in the immediate vicinity, and the bluish-brown appearance of the solid nodule as it is brought into view.

Single metastatic nodules—Any discrete nodule in the neck which is hard and partially fixed and of recent origin must be considered a metastatic node until proved otherwise.

Upper metastatic nodes usually drain from primary lesions in the nasopharynx. Fully 10 per cent of patients with a metastatic nodule in the neck from a primary lesion in the pharynx or larynx will be unaware of the primary growth, but will complain of a "lump in the neck." It therefore becomes necessary first to make a meticulous search of the nasopharynx, oral cavity and larynx before attacking the neck node.

With lower nodules, search should be made particularly for lesions in the thyroid, but any nodule in the neck may have its primary growth anywhere below the clavicle.

Unless a primary lesion is found, a biopsy should always be made as it not only may offer a clue to the location of the original growth, but it also may be a guide for treatment.

Cystic hygromas—Cystic hygromas are due to sequestration of lymphatic vessels which have not found their connection with the main ducts. Although these cysts may be found anywhere in the body, they are most common in the neck and most often located in the supraclavicular area (figure 13). Cystic hygromas are almost always multilocular. In contrast with branchial cysts, they are very soft and flabby, will transmit light, and the aspirated contents consist of straw-colored fluid which frequently congeals on exposure to air. The fluid may be of a brownish color from previous hemorrhage. I have aspirated some in which one cyst contained the straw-colored fluid, while an adjacent one had a brownish or frankly bloody fluid.

These cysts may be localized but many are invasive, with many smaller cysts in the fascial planes of the neck, and with cystic masses completely surrounding the large vessels with extension of the growth into the mediastinum or down the arm (figures 14 and 15).

Salivary gland tumors—About 90 per cent of salivary gland tumors occur in the parotid and only 10 per cent in the submaxillary gland. The mixed parotid tumor is by far the most common type. Marshall of the Lahey Clinic reported malignancy in 27 of 213 patients with mixed parotid tumors, an incidence of roughly 13 per cent.

The diagnosis of mixed tumors of the parotid should not be too difficult. The differential diagnosis between benign and malignant tumors may be difficult or impossible without a biopsy. A movable encapsulated tumor is likely to be benign. Because of the structure

FIGURE 13. Cystic hygromas are usually located in the supraclavicular area. They are usually multilocular, soft and transmit light. Contents of the cyst are clear lemon-yellow in color.

FIGURE 14. Cystic hygroma may be extensive. The infant's neck is entirely filled and the mass fills the mediastinum as well. This is a cervicomediastinal cystic hygroma.

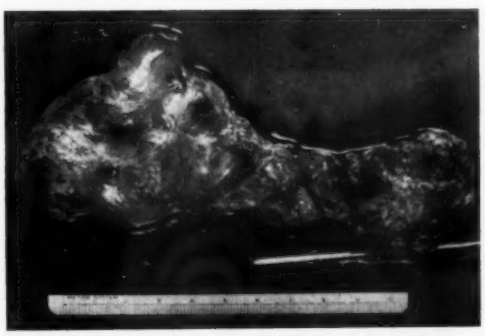

FIGURE 15. Excised specimen removed from the neck of the infant shown in figure 14. Many cysts have already been punctured. The probe is in the internal jugular vein which had to be sacrificed.

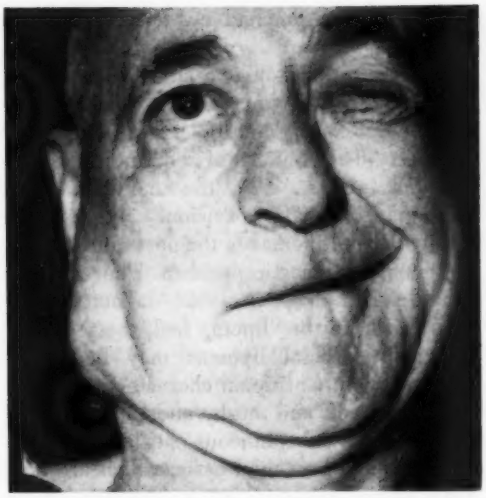

FIGURE 16. Mixed parotid tumor. Rapid growth, pain and, particularly, facial nerve involvement (without previous surgery) are signs of malignancy.

of the parotid, fixation is, however, not necessarily a diagnostic factor. A tumor can, however, be suspected of being malignant when it has a history of rapid growth, when there is pain, and, particularly, when there is facial nerve involvement without previous surgery (figure 16).

Patients with mixed tumors of the submaxillary gland usually present themselves with a slow-growing tumor beneath the jaw. Those in the posterior portion of the submaxillary gland may be differentiated from those of parotid origin only with difficulty, but examination with one finger in the mouth and one on the tumor may detect its location. Where the entire submaxillary gland is enlarged and tender, the possibility of a duct stone must be ruled out, and where the tumor is not encapsulated, the diagnosis of lymphosarcoma must be considered.

Dermoid cysts—Dermoid cysts may occur laterally as well as medially. They should not be confused with sebaceous cysts, which are always attached to the skin. Dermoid cysts are unilocular, although there may be several, and they have a characteristic doughy feeling if superficial enough to be palpated. They may readily be confused with lipomas, and par-

ticularly with branchial cysts, if situated in the upper third of the neck or in the classic location of a branchial cyst. A soft, flabby, multilocular, light-transmitting, cystic hygroma should not be a problem in differential diagnosis. The contents of a dermoid cyst are too thick to aspirate, but the final diagnosis is often made only after excision.

Lipomas—Lipomas in the posterior triangle present no diagnostic problem. They may be superficial or deep, are soft, do not contain fluid and have the "lipoma feel," so to speak. Lateral superficial lipomas may be distinguished by an additional characteristic: They are usually soft and mushy and can be picked up as distinct subcutaneous entities in contradistinction to branchial cysts, which are held down by the investing fascia. The skin over a lipoma may be wavy, as over lipomas in other parts of the body. Aspiration does not yield anything. They are not as circumscribed or encapsulated as are dermoid cysts and do not have a doughy consistency. They do not contain fluid or transmit light as do cystic hygromas. A deep growth may present itself as a firm swelling, not distinguishable from a deep cyst; fortunately, the deep growths are rare.

Neurofibromas—A neurofibroma must be considered in the case of any tumor which is very hard but well circumscribed, somewhat elongated and located in the region of a major nerve. In the neck, the hypoglossal, vagus and accessory nerves are occasionally so involved. The diagnosis of neurofibroma can be established in surgery by examining the ends of the tumor and finding the entrance and exit of the main trunk of the nerve.

Hemangiomas—Superficial hemangiomas are readily recognized. The deep tumors present diagnostic problems as they do not have fixed boundaries. There are several tests which might provide a clue: Deep hemangiomas usually can be reduced in size by pressure over the growth. By placing the patient in a steep Trendelenburg position the hemangioma may distend. It will also enlarge when the patient forcefully inhales against the closed glottis. They tend to contain phlebolites and an x-ray should be taken to detect their possible presence when a hemangioma is suspected.

Cervical Lymphadenopathies

We shall divide those tumors which are of lymph node origin into two groups. The first group comprises those lymph node enlargements which are neoplastic. In the second group are those lymphadenopathies which are inflammatory due to various infections.

Primary Lymphatic Tissue Tumors

Lymphomas—There are many classifications in this group and much confusion about them exists among practitioners as well as among pathologists.

Lymphoid tumors represent neoplastic outgrowths of various cells comprising the normal lymph node. The degree of malignancy is as variable as the classification. The confusion regarding these tumors is no doubt due to their unstable behavior. Carver, of Memorial Hospital, states that a node from one patient may seem histologically a sarcoid, but a few months later, a biopsy specimen may indicate Hodgkin's disease, and again, at a later date, a biopsy may show reticulum cell sarcoma.

A biopsy should be done of any enlarged node lasting three weeks, without obvious source, and without a leukemic blood picture.

What are some of the various classifications? I shall list but two. The lymphoma classification, as given by Young of the Lahey Clinic, is as follows:

1. Macrofollicular lymphoma
2. Malignant lymphocytoma
3. Lymphosarcoma
4. Reticulum cell sarcoma
5. Hodgkin's disease

The classification given by Ward and Hendricks is as follows:

1. Hodgkin's granuloma
2. Lymphosarcoma
3. Reticulum cell sarcoma
4. Giant follicle lymphoma
5. Lympho-epithelioma

I shall discuss briefly the two most common lymphomas, namely, Hodgkin's disease and lymphosarcoma.

Hodgkin's disease—In Hodgkin's disease there is a progressive enlargement of the lymph nodes. They are at first discrete, rubbery and movable; later they form a conglom-

erate mass of nodes. The nodes are not tender. These patients may at first have normal blood counts, with possibly some leukocytosis, but as the disease progresses there is an anemia with a leukopenia, increasing malaise and bouts of a low grade remittent fever, the so-called Pel-Ebstein fever. The spleen frequently becomes enlarged as the disease progresses. The diagnosis must be made by biopsy of a node. The finding of a characteristic giant cell, the Sternberg-Reed cell, establishes the diagnosis.

Lymphosarcomas—Lymphosarcomas are second in occurrence to Hodgkin's disease among the primary diseases of the neck. Stout has classified them as follows:

1. Reticulum cell lymphosarcoma
2. Lymphatic cell lymphosarcoma
3. Giant follicle lymphosarcoma

The primary lesion has a less definite outline than in Hodgkin's disease, and it may rapidly produce a rather bulky growth. These tumors have true metastases. They are extremely invasive and destructive, developing obstructive symptoms from pressure on the trachea, esophagus and blood vessels. Irradiation is at times highly effective for this group of tumors.

Lymphadenitis, Inflammations and Infections

Lymph node enlargement may be encountered in the following inflammatory and infectious diseases.

Acute suppurative lymphadenitis—There is usually an abrupt onset following a sore throat or other oral infection. There are tenderness and signs of inflammation in which the tonsillar nodes are usually involved.

Chronic cervical lymphadenitis—Usually several nodes are involved. The condition is almost limited to young children. A possible focus may be present. Diagnosis is impossible without biopsy. At the Memorial Hospital, this has been nicknamed by Carver "The Upper New York State Disease."

Infectious mononucleosis—This is an acute generalized infection. The lymphocytes are relatively increased and are toxic. There is often enlargement of the spleen. The diagnosis is made by the heterophil agglutination test. A dilution of 1 to 8 is normal; 1 to 30 is suggestive; 1 to 120 is absolute.

German measles—The rash may be so slight that it is overlooked. The posterior triangle and posterior auricular nodes are involved. The nodes are not over 1 cm. in size and disappear in a few days, or at most in two weeks.

Tuberculosis—Formerly quite common, the incidence of tuberculosis is now declining, at least in this country. General improvement of health and pasteurization of milk may have been factors in this decline. Tuberculous nodes are at first discrete, but later conglomerate. The skin over the nodes may become adherent. The glands may break down, causing chronic draining sinuses. If the discharge is caseous, the diagnosis may be obvious. A biopsy of the tissue of the sinus, or of the node, will establish the diagnosis, and guinea pig inoculation of pus is advisable. In young children a tuberculin skin test will also provide a clue.

It must be emphasized that these patients do not necessarily have true pulmonary tuberculosis; in fact, most of them do not.

Syphilis—This disease is becoming much less common, to the point of extinction. Nevertheless, a primary lesion of the mouth or face will produce lymph node enlargement in the neck. There is generalized lymphadenopathy in the second stage with lymphocytosis, eosinophilia and a positive serology.

Actinomycosis—The sulfur granules of the discharge establish the diagnosis.

Brucellosis—Enlarged lymph nodes do accompany undulant fever. The organisms may be recovered from the blood stream. An agglutination titer above 1 to 40 is considered diagnostic.

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Physiologic Considerations in Parenteral Fluid Therapy

EDMUND C. BURKE*

Mayo Clinic, Rochester, Minnesota

EDMUND C. BURKE

WATER and electrolyte physiology is a comprehensive subject. Physicians find it difficult to understand the complexities of ions and the factors governing their activities. The knowledge of a few sound physiologic facts about fluid therapy may serve the physician in good stead in his approach to diagnosis and therapy of electrolyte disorders.

An effort will be made to present a few fundamental concepts of fluid therapy. Emphasis will be placed on certain aspects of renal physiology as they are related to electrolyte disorders. Consideration will be given to the role of sodium, potassium, chloride, dextrose and water in body physiology and to the principles governing their use in fluid therapy.

*Section of Pediatrics, Mayo Clinic, Rochester, Minnesota.

Renal Function

The kidney assumes a more important role than any other organ of the body in the physiology of salt and water. This organ possesses the remarkable ability to retain or excrete water and electrolytes to protect that constancy of the internal environment designated as homeostasis.

The kidney has two functioning units, the glomeruli and the tubules. The glomerulus is simply a capillary mass which mechanically filters 25 per cent of the cardiac output to produce about 180 liters of filtrate daily. Urea, phosphates, sulfates and organic acids are removed from the blood by glomerular filtration.

The glomerular fluid is a protein-free, ultrafiltrate of plasma having the same acid-base ratio as the plasma, that is, a pH of 7.4. The rate of glomerular filtration is relatively constant, although the rate of blood flow through the glomeruli and the number of functioning glomeruli may vary from time to time.

The tubules play a vastly different role for they reabsorb all but 2 liters of the fluid.

They are able to reabsorb or excrete ions across the membrane of the tubule cell to acidify or to alkalize the urine. The limits of urinary acidity and alkalinity vary from a *p*H of 4.5 to a *p*H of 7.8 as determined by the metabolic needs and the efficiency of renal function.

Glomerular filtrate, being slightly alkaline with a *p*H of 7.4, contains a phosphate with two sodium ions in the molecule, or, disodium phosphate. It is postulated that a hydrogen ion within the tubule cell is exchanged for one of the sodium ions of the phosphate molecule. The result is monosodium phosphate, an acid substance. Potassium may compete with sodium for exchange with the hydrogen ion, or at times a potassium ion may be secreted into the fluid from the tubule cell.

Figure 1 depicts diagrammatically[1] the ion exchange. Carbonic anhydrase (C.A.) is an enzyme which catalyzes water and carbon dioxide to carbonic acid. It can be seen that half of the base in glomerular filtrate can be returned to the blood and become available as an important buffer base, namely, sodium bicarbonate.

The efficiency of acidification of the tubular fluid by the cells of the tubules is measurable as titratable acidity (T.A.).[2,3] Titratable acidity is determined by titrating against the acid phosphate with a tenth-normal solution of sodium hydroxide to a *p*H of 7.4. In an alkaline urine, therefore, by definition one does not have any titratable acidity.

The production of ammonium (NH_4) comprises a second and more efficient means of renal conservation of base. I recently carried out a simple study to demonstrate the production of ammonium and titratable acidity by administering ammonium chloride, an acid salt, to a normal 7 kg. infant.* Figures 2 and 3 and tables 1 and 2 show the resulting changes in the concentration of the serum, in the body weight, and in the chemical composition of the urine.

A third aspect of tubular function concerns the conservation of water. Depending on the amount of substances or solutes to be excreted, the kidney draws on the water stores of the body. The concentration of the urine is

*This study was done under the supervision of Dr. W. M. Wallace at the Children's Hospital, Boston, Massachusetts.

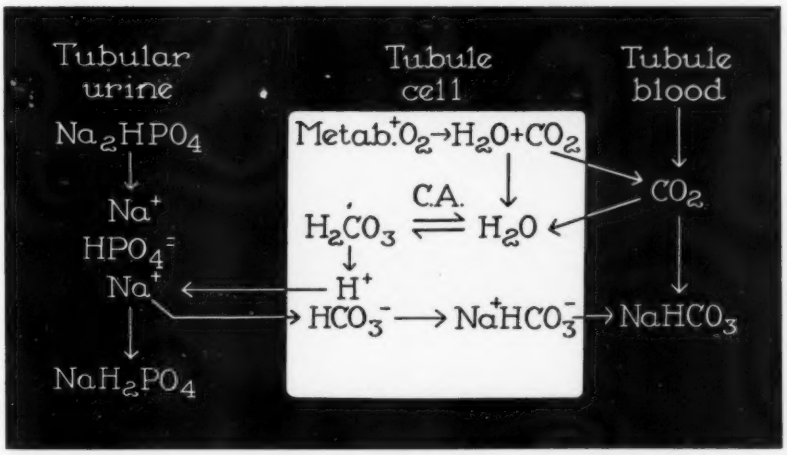

FIGURE 1. Diagrammatic representation of the exchange of a hydrogen ion for a sodium ion. The alkaline disodium phosphate is changed to an acid salt, monosodium phosphate, through the loss of a sodium ion and the addition of a hydrogen ion. Carbonic anhydrase (C.A.) catalyzes the reversible reaction between water and carbon dioxide. The base, sodium bicarbonate, is returned to the blood. (Adapted from Pitts and Alexander.[1])

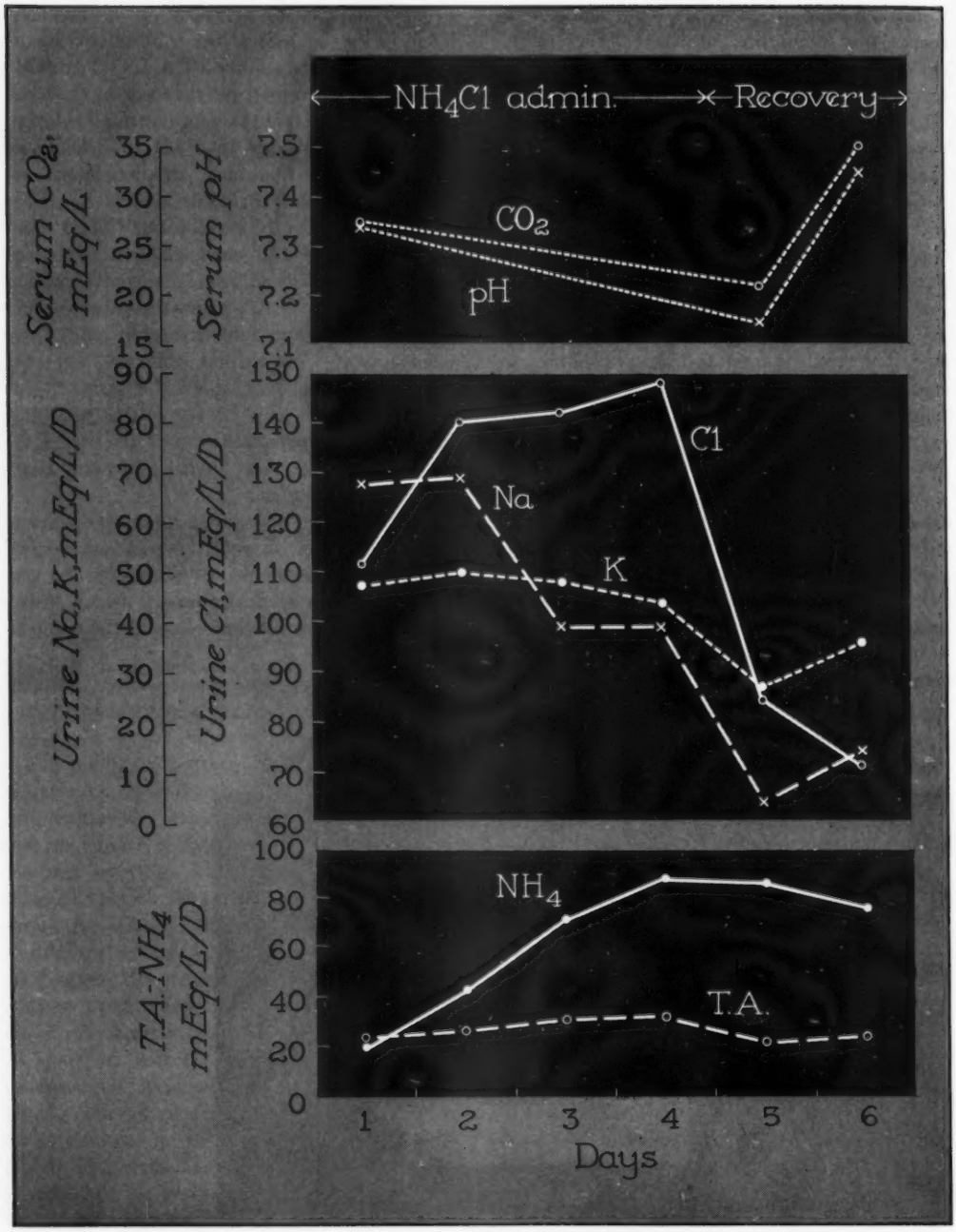

FIGURE 2. *The uppermost graph* shows changes in carbon dioxide and the pH of the serum during and after electrolyte loading with ammonium chloride. *The center portion* depicts changes in urinary sodium, potassium and chloride during the study. The determinations were made on 24-hour specimens of urine. *The lowermost portion of the graph* represents ammonium production and titratable acidity in mEq. per liter per day.

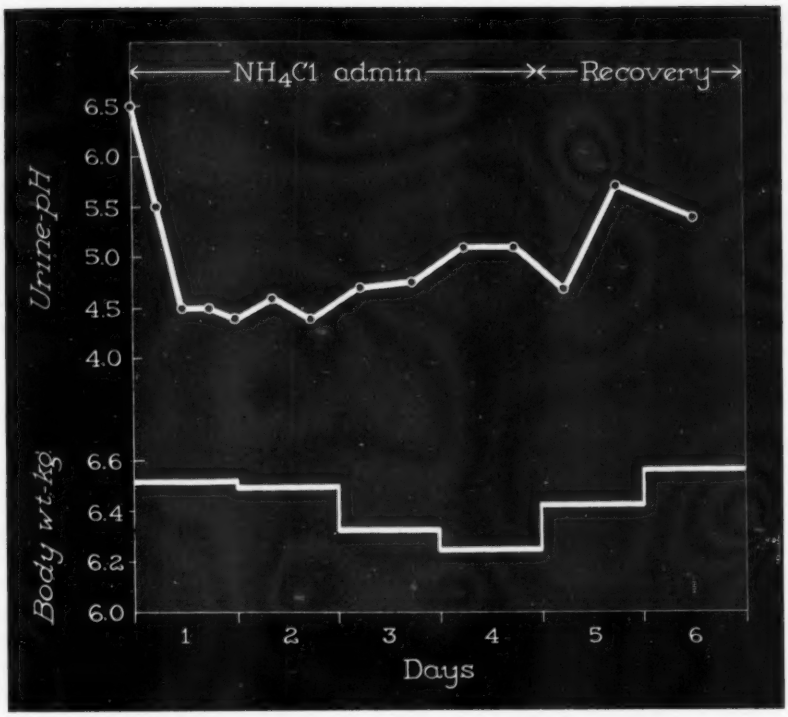

FIGURE 3. Changes in *p*H of the urine and body weight during administration of ammonium chloride and during recovery.

measured in terms of specific gravity. If the amount of solutes for excretion is great or if the demand for conservation of body water is great, the urine will be highly concentrated. Loss of water from the body by other routes naturally results in a decrease of the available water for renal function.

The minimal volume of water required for the formation of urine is termed the "renal obligatory need." In an adult, the maximal concentration ability of the tubules usually defines the renal obligatory water need as approximately 700 cc. daily. If this volume of water is not available, oliguria or anuria follows. Even in starvation or thirsting, the renal obligatory need must be met, or renal failure will occur.

As a result of the renal mechanisms just described, glomerular disease may result in the retention of nitrogenous compounds and the subsequent development of azotemia or uremia. Failure of the renal tubules, on the other hand, may exist together with, or independently of, glomerular integrity. Tubular failure may be evidenced by the production of large volumes of urine with an alkaline *p*H and a low specific gravity. It becomes obvious that good management of a fluid and electrolyte problem requires close observation of the volume, specific gravity, and *p*H of the urine.

Water

The water content of the body approximates 70 per cent.[4] Fifty per cent of the body water resides within the cells and is designated as "intracellular water." The "intracellular compartment" is relatively constant and gives up its water only under conditions of dire stress.

Of the remaining 20 per cent, 5 per cent is contained in the vascular system and 15 per

cent resides interstitially. This 20 per cent fraction of body water is designated as the "extracellular water." In infants and children, 25 per cent of the water is extracellular water. In the presence of edema, the extracellular space increases. Conversely, if dehydration is present, the extracellular space decreases.

Loss of body water occurs principally by three routes: (1) by the skin, (2) by the lungs, and (3) by the kidneys. Except in the presence of diarrhea, loss of water in the stools is negligible.

The water lost from the lungs and skin is designated as "insensible loss." Perspiration represents sensible or visible loss. Fever and hyperpnea cause an increase in the loss of body water. When excess water is lost extrarenally, the daily requirements for water increase. If the extra demands for water are not met, oliguria or anuria will result.

Table 3 shows the aqueous requirements for persons of various ages as well as the amounts of water lost by the different routes.

Excessive administration of water, whether

TABLE 1

URINARY ELECTROLYTES DURING AND AFTER LOADING WITH AMMONIUM CHLORIDE

DAY*	VOLUME (cc.)	pH	URINARY CONSTITUENTS, mEq. PER LITER					NH_4/T.A.
			Na	K	Cl	NH_4	T.A.†	
1	635	6.5 5.5 4.5	67.6	47.4	112	20.4	23.7	0.86:1
2	596	4.4 4.6 4.4	69.1	50.0	140	43.4	27.1	1.60:1
3	516	4.7 4.78	39.9	48.0	142	71.4	31.9	2.24:1
4	572	5.1 5.1	39.9	44.0	148	88.4	32.6	2.71:1
5	470	4.7 5.7	4.5	27.0	84	86.9	23.1	3.76:1
6	475	5.4	14.7	36.0	72	76.6	26.0	2.94:1

*Ammonium chloride, 10 mEq. per kilogram of body weight per day, was given on days 1 through 4.
†T.A. = titratable acidity.

TABLE 2

SERUM ELECTROLYTES BEFORE AND AFTER LOADING WITH AMMONIUM CHLORIDE

DAY*	SERUM					BODY WEIGHT (kg.)	INTAKE (cc.)
	pH	CONSTITUENTS, mEq. PER LITER					
		CO_2	Na	K	Cl		
1	7.35	27.00	142	5.70	104	6.52	1078
2						6.50	979
3						6.33	995
4						6.25	1030
5	7.22	17.24	147	5.11	125	6.43	1118
6	7.50	32.62	148	5.05	102	6.57	1260

*Ammonium chloride, 10 mEq. per kilogram of body weight per day, was given on days 1 through 4.

TABLE 3

DAILY LOSS AND REQUIREMENTS OF WATER

AGE GROUP	WATER LOSS (CC.) PER DAY				USUAL ALLOWANCE (cc.)*
	Urine	Stool	Insensible	Total	
Infants	200- 500	25- 40	75- 300	300- 800	125
Children	500- 800	40-100	300- 600	800-1500	75
Adults	700-1000	100	600-1000	1500-2000	45

*Per kilogram of body weight per day.

by the oral or parenteral route, can produce water intoxication, a particularly dangerous clinical syndrome. When this occurs, the extracellular compartment is so extended as to produce a dilution of the serum. Convulsions and even death have been observed as the consequences of water intoxication.

It is possible for water intoxication to occur even when the total amount administered is not great or when the rate of administration is not excessively rapid. Awareness of the possibility of water intoxication can forestall its occurrence.

Vomiting, diarrhea, thirsting, nasal suction, inadequate intake, renal disease and diabetic acidosis are causes of dehydration. Dehydration may occur with or without excessive loss of electrolytes. Therapy for dehydration consists of replacement of water, usually as dilute electrolyte solutions containing dextrose.

Sodium and Chloride

The normal concentration of sodium in the serum is 135 to 142 mEq. per liter. Sodium resides principally extracellularly. The body possesses a large reservoir of sodium in the bones, and this is available in times of stress. Metabolic acidosis can result when excessive loss of sodium occurs. The carbon dioxide combining power of the plasma, which normally is 27 mEq. per liter, will be low as a result of a compensatory effort to make the total acid ions (anions) balance the depleted base ions (cations).

Diabetic acidosis is one of the major causes of depletion of sodium, but diarrhea and renal disease likewise produce marked depletion of sodium.

Chloride is an extracellular acid ion (anion) which frequently is lost in conjunction with sodium in various metabolic states. The concentration of chlorides in the serum ranges from 90 to 103 mEq. per liter. Vomiting may produce a large loss of chlorides, which frequently is in excess of the loss of the companion ion sodium. In cases of pyloric stenosis, an increase in the carbon dioxide combining power of the plasma represents an attempt to balance the relative excess of sodium and the deficit of chlorides in the serum. Excessive loss of both sodium and chlorides by profuse perspiration may result in "miner's cramp."

In so-called physiologic saline solution, the concentration of sodium and of chlorine is 154 mEq. per liter. Since the concentrations of these ions are in excess of those in the serum, two-thirds of the water in the saline solution is required by the kidneys to excrete the excess of sodium and chlorides.

It is apparent that the administration of physiologic saline solution is hardly the treatment of choice for dehydration. It is more physiologic to use a solution made up of 2 parts 5 per cent solution of dextrose, 2 parts water and 1 part physiologic saline solution.

Table 4 shows the amount of sodium chloride or physiologic saline solution required daily by patients in different age groups. It will be noted that infants require only 1 gm. of sodium chloride or 125 cc. of physiologic saline solution per day. Undiluted saline solution has little place in the treatment of children, and it rarely should be administered parenterally to premature infants because it is likely to cause edema.

TABLE 4

DAILY REQUIREMENT OF SODIUM CHLORIDE OR PHYSIOLOGIC SALINE SOLUTION

AGE GROUP	NaCl *(gm.)*	PHYSIOLOGIC SALINE SOLUTION *(cc.)*
Infants	1	125
Children	3	350
Adults	6	700

Potassium

The human body contains approximately 175 gm. of potassium. Ninety-eight per cent of this amount is situated within the cells; the remaining 2 per cent is found in the serum. The normal concentration of serum potassium is 4 to 5 mEq. per liter.

Two-thirds of the potassium in the cells is protein bound while the remaining third is free to migrate in and out of the cells. An increase in the concentration of the hydrogen ion or an extracellular lowering of the *p*H causes a migration of the cation potassium out of the cells. Presumably, this migration represents an attempt to neutralize the extracellular acidity.

Sodium and potassium have an intense aversion for each other. When sodium is given to a patient it causes an increase in excretion of potassium. Administration of excessive amounts of sodium without potassium may cause signs of hypokalemia.

The low potassium syndrome (hypokalemia) is manifested by abdominal distention, ileus, mental confusion, a fall in blood pressure, muscle paralysis, and at times by death. Electrocardiography is helpful in detecting the presence of this condition, although the correlation between the serum potassium and the electrocardiographic tracing is not absolute. The electrocardiogram is more representative of the potassium content of the cells of cardiac muscle.

Classic electrocardiographic changes in cases of hypokalemia are flattening or inversion of the T wave and lengthening of the Q-T interval. Electrocardiography is a useful tool for following the effects of the intravenous administration of vitamin K.

Potassium depletion may occur as the result of an inadequate oral intake of this element, severe diarrhea, continuous suction of gastric or intestinal secretions, prolonged vomiting, ileostomy or diabetic acidosis. The excessive intake of sodium, as previously mentioned, also may provoke signs of potassium deficiency.

In the treatment of potassium deficiency, 3.5 mEq. per kilogram of body weight may be administered daily by the intravenous route without danger of causing heart block or signs of potassium intoxication. The solution should not contain more than 35 mEq. of potassium per liter and should be given slowly. Great caution must be exercised when solutions of potassium are given intravenously to patients with impaired renal function, since the majority of potassium is excreted in the urine. Ideally, oral administration of potassium is to be preferred to administration by the intravenous route.

Hyperkalemia is encountered less frequently, but it may be detected by the electrocardiographic changes, heart block or paresthesia. Death may result from potassium intoxication. In potassium intoxication the characteristic electrocardiographic changes include peaking of the T wave and shortening of the Q-T interval.

Potassium metabolism and dextrose metabolism are undoubtedly closely related, since it has been observed that the administration of solutions of dextrose decreases the concentration of potassium in the serum while the content of this ion in the cell increases. Hypokalemia may be precipitated by administering solutions of dextrose without potassium.

Dextrose

Several salient features of dextrose metabolism have already been mentioned; namely, the provision of water for renal function by metabolism of the carbohydrate, and the association of carbohydrate and potassium metabolism. Dextrose also exerts a protein-sparing effect during the breakdown of tissues or during the catabolic activity of starvation. Daily administration of 100 gm. of dextrose by the oral or intravenous route will

produce the maximal protein-sparing effect, and the administration of larger doses will not have any additional effect.

Since 1 gm. of dextrose provides only 4 calories, it is impractical to try to meet the caloric requirements of the body by administering this carbohydrate intravenously. The use of protein hydrolysates will provide additional calories and also will supply amino acids. It should be pointed out, however, that unless preparations of fat can be administered it is hardly possible to meet the caloric requirements by intravenous administration without causing edema or water intoxication. If the caloric requirements cannot be provided by the intravenous route, it is not possible to change the metabolic state of the patient from the catabolic to the anabolic phase unless oral feedings can be given.

Planning the Therapeutic Program

When confronted with an electrolyte problem one should determine the basic cause of the disturbance. One must determine whether the disturbance involves loss of water, electrolytes or both. Usually, both water and electrolytes have been lost.

It is important to estimate the rate at which the disturbance has progressed, since the homeostatic mechanisms will attempt to maintain metabolic equilibrium during the course of the illness. One must not attempt to correct the disturbance too rapidly because this may aggravate the patient's condition.

Lastly, the status of renal function is of vital importance inasmuch as renal function may be such that the patient cannot tolerate the water and electrolytes provided intravenously. For example, it would be foolhardy to give excessive amounts of water or potassium in the presence of anuria. Efforts may be limited to the provision of amounts of fluid to compensate for insensible loss and loss in the stools.

The daily weight of the patient is of invaluable aid in detecting the early development of edema or dehydration. It is usually rather easy to obtain the daily weight in following the progress of infants.

It appears more physiologic to employ solutions slightly more hypotonic than the body fluids and to allow for the mechanisms of the body to retain that which is needed and to excrete that which is not.

The so-called 1:2 solution (a solution containing 1 part of physiologic saline solution and 2 parts of a 5 per cent solution of dextrose) and the so-called 1:2:3 solution (a solution containing 1 part of a sixth-molar solution of lactate, 2 parts of physiologic saline solution and 3 parts of a 5 per cent solution of dextrose) are of practical value. A liter of sixth-molar solution of lactate contains 167 mEq. of sodium and a similar amount of lactate.

According to Talbot, Crawford and Butler,[5] four times as much hypotonic solution as physiologic saline solution can be administered intravenously without danger of edema from renal inadequacy.

If the volume of solution that is administered intravenously is midway between that required to supply the minimal requirements of the body and that required to supply the maximal requirements it will not interfere with the ability of the kidney to excrete water and electrolytes.

For preparing solutions for intravenous administration, it is possible to obtain ampules that contain 20 mEq. of potassium chloride. One should try to "tailor" the solution to the needs of each patient rather than resort to the haphazard administration of any solution that may be available.

Summary

The vital role of the kidney in the maintenance of fluid and electrolyte equilibrium suggests that knowledge of renal function should prove useful to the physician in the management of electrolyte disorders.

Conservation of base and water and excretion of nonutilizable end products of metabolism are intimately related to homeostasis. The excretion of organic acids, urea, phosphates and sulfates is accomplished by glomerular filtration while the ion exchange mechanism, production of ammonium and conservation of water are the result of tubular activity. Tubule cells are actively engaged

in excretion, secretion and reabsorption.

Water content of the extracellular compartment fluctuates widely and rapidly during various metabolic disorders. The water content of the largest compartment, the intracellular space, is affected only in cases of prolonged metabolic disturbances.

Water intoxication is the result of dilution of body fluids at a more rapid rate than can be compensated for by homeostatic mechanisms. Excessive parenteral administration of sodium, potassium or chloride can lead to serious clinical syndromes and even death.

Administration of potassium in large quantities should be carried out cautiously and preferably with the information obtained by electrocardiography and chemical examination of the serum. Anuria is usually a contraindication for administration of potassium.

One should give careful consideration to certain important features of an electrolyte disturbance such as duration of illness and nature of the deficit. An illness of long duration should not be corrected rapidly. Similarly, dehydration should not be treated with hypertonic solutions of electrolytes.

The use of hypotonic solutions of dextrose containing sodium, chloride, potassium or other ions is advised because of the wide margin of safety provided to renal function.

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MEETINGS *and Postgraduate Courses*

American Institute of Dental Medicine: Annual meeting at the Desert Inn, Palm Springs, California October 31-November 4, 1954. Further information may be obtained from the Executive Secretary, Miss Marion G. Lewis, 2240 Channing Way, Berkeley 4, California.

National Gastroenterological Association: Sixth annual course in postgraduate gastroenterology at The Shoreham in Washington, D.C., October 28-30, 1954. Co-chairmen will be Dr. Owen H. Wangensteen, Professor of Surgery of the University of Minnesota Medical School and Dr. I. Snapper, Director of Medical Education, Beth-El Hospital, Brooklyn, New York. For further information and enrollment write: National Gastroenterological Association, Department GSJ, 33 West 60th Street, New York 23, New York.

Inter-Society Cytology Council: Second annual meeting at the Statler Hotel in Boston, November 12-13, 1954. Additional information may be obtained from the Secretary-Treasurer, Inter-Society Cytology Council, 634 North Grand Blvd., St. Louis, Missouri.

GENERAL PRACTICE *Review*

This department offers the latest, proved methods for the treatment and management of commonly encountered conditions based on the extensive experience of the physicians who prepare these summaries for POSTGRADUATE MEDICINE.

Cholecystitis

GEORGE F. O'BRIEN*

Stritch School of Medicine of Loyola University, Chicago

GEORGE F. O'BRIEN

DISEASES of the gallbladder together with those of the biliary tract are responsible for a significant number of abdominal complaints. The causes of biliary tract disease include congenital abnormalities, infection, vascular disturbances and malignant disease. In addition to these etiologic factors common to practically all structures of the body, the biliary tract falls heir to a special type of pathology incident to the presence of calculi.

Etiology and Pathology

The most common disease of the gallbladder is cholecystitis. This condition may present itself in an acute, subacute or chronic form. Much confusion has existed regarding the pathogenesis of cholecystitis. As the name implies, infection was initially considered an important factor. Bacteriologic studies of bile and the gallbladder walls in the presence of cholecystitis have yielded surprisingly few positive cultures. Similarly, pathologic changes in the walls of gallbladders removed because of cholecystitis are not entirely consistent with those considered characteristic of infection.

If bacteria are not the primary cause of cholecystitis, it must result from disturbances in gallbladder physiology or in the nature and character of gallbladder bile. Experimentally, changes similar to those observed in cholecystitis have been produced by obstructing the cystic duct, by subjecting the gallbladder mucosa to the effects of concentrated bile, and by impairing the blood supply to the gallbladder. These conditions are all operative in acute cholecystitis. A small calculus impinges on the cystic duct, producing spasm and edema of the gallbladder neck. Depending on the

*Chairman, Department of Medicine, Stritch School of Medicine of Loyola University; Head of Department of Medicine, Mercy Hospital, Chicago, Illinois.

degree of spasm and edema, the blood vessels of the area become more or less obstructed. There will be interference with venous and lymphatic drainage from the gallbladder. The gallbladder wall becomes edematous, the veins dilate allowing red cells to escape into the perivascular space, and the tissues undergo changes incident to the degree of anoxia that is produced.

In addition to these vascular changes, further damage occurs from the chemical effect of the concentrated bile. The more concentrated the bile and the greater the vascular changes, the more damaging are the effects. So long as cystic duct obstruction and impairment of blood supply persist, destructive processes continue in the gallbladder wall. These may reach the stage of focal necrosis, and occasionally go on to perforation within a period of 48 to 72 hours. Generally there is a fibrinous reaction on the gallbladder serosa, causing it to become adherent to surrounding structures. These fibrinous adhesions between the gallbladder and adjacent viscera undoubtedly prevent many dangerous perforations while adding to the difficulties of the surgeon who removes the quiescent gallbladder. Because of the nature of the pathology during the acute phase of cholecystitis, removal presents technical risks to even the most skilled surgeon. The wall is friable, intensely hyperemic and edematous and is markedly susceptible to infection.

Infection probably occurs when the bile contains bacteria or when bacteria reach the gallbladder wall by way of lymphatic channels. When secondary infection is a prominent feature in acute cholecystitis, necrosis of the gallbladder becomes imminent and empyema is always a possibility.

Fortunately the acute destructive process associated with cholecystitis usually begins to subside in about 48 hours. Presumably the cystic duct obstruction ceases and the gallbladder circulation is restored. The edema subsides, necrotic material is removed and fibrosis ensues. If repeated attacks occur the gallbladder may become a shrunken, thick, fibrous structure, often snugly stretched over luminal calculi. Occasionally these calculi produce a necrosis of the gallbladder wall and adherent viscera. Should stones enter the small bowel, they may lead to an obstruction.

Symptoms and Diagnosis

The diagnosis of acute cholecystitis is usually quite definite. According to Cole, 32 per cent of women and 16.2 per cent of men past the age of 40 years have gallstones; however, only about one-third of these patients present any symptoms. Although uncommon, it is possible for young children to have acute cholecystitis. The clinical picture of cholecystitis can be divided roughly into dyspeptic and painful symptoms.

The dyspeptic symptoms occur in chronic cholecystitis and are related to disturbed functions in the gastrointestinal tract. There may be pylorospasm leading to delayed emptying of the stomach with resultant belching, nausea or even vomiting. Disturbed motility of the bowel, either reflex or because of bile deficiency, may cause diarrhea or constipation. A sensation of bloating soon after eating, together with epigastric distress and colonic pain, are probably expressions of altered gastrointestinal physiology. The aggravation of dyspeptic symptoms by animal fats is further evidence of disturbed intestinal enzymatic activity caused by an inadequate and altered intestinal bile content. These dyspeptic symptoms may be present most of the time or may appear only after certain dietary indiscretions. By themselves, dyspeptic symptoms indicate simply a disturbance in function of the gastrointestinal tract. Gallbladder disease is only one of the causes that must be considered.

Pain is the most common symptom of cholecystitis, particularly in the acute and subacute forms. It may be located anywhere in the upper abdomen. In order of frequency, pain occurs in the right upper quadrant, in the epigastrium, and in the epigastrium and left upper quadrant. Infrequently, it is present only in the left upper quadrant or over the precordium. The duration of the pain is quite variable. It usually occurs in attacks lasting from 15 minutes to two or three hours. If the pain persists over several hours, the possibility of a developing empyema of the gall-

bladder must be considered. Pain occurring solely in the left upper quadrant must be differentiated from that produced by acute pancreatitis. Early measurement of serum amylase should be made when pancreatitis is suspected, and might profitably be obtained in all patients with acute upper abdominal pain.

Occasionally the pain associated with cholecystitis is experienced over the precordium. When this occurs the patient may be considered to have coronary heart disease. Electrocardiograms taken during an attack of cholecystitis often reveal abnormalities that further suggest cardiac origin for the pain. In most instances when precordial pain is associated with gallbladder disease, there is a definite chronic coronary sclerosis which is undoubtedly the source of the precordial pain. When precordial pain exists along with tenderness over the gallbladder area, it may be difficult to reconcile their relationship. Precordial pain has been relieved by cholecystectomy in a sufficient number of patients to postulate a relationship between the diseased gallbladder and coronary pain. Transitory electrocardiographic changes were recently observed in a patient with precordial pain and empyema of the gallbladder. Following surgical treatment of the gallbladder, the electrocardiogram quickly returned to normal.

With acute episodes of cholecystitis, nausea and vomiting are early symptoms that occur persistently or intermittently for several days. The vomitus, at first light-colored, becomes quite bile-tinged as the patient begins to vomit duodenal contents. Fever usually accompanies acute cholecystitis and may range from 100° to 103° F.

Physical examination during an acute attack reveals localized tenderness over the gallbladder. Depending on the amount of peritoneal irritation, there will be a certain degree of rigidity in the right upper abdominal quadrant. Rarely, the gallbladder is actually palpable. Icterus is absent to faint unless there is an associated common duct obstruction. Leukocytosis is usually present and when found to be increasing, along with persistent right upper quadrant tenderness and rigidity, suggests the possibility of developing empyema of the gallbladder. It has frequently been said that blood in the stool in the presence of jaundice is strong evidence of carcinoma of the biliary tract. Hudson and Johnson reported blood in the stools of 13 per cent of the patients with cholecystitis. Further, Christopher recorded 28 patients who had experienced massive hemorrhage from the gallbladder. Sclerotic changes in the gallbladder wall together with erosions of the wall, and possibly of the cystic artery, by calculi have been considered the probable cause of bleeding.

Cholecystograms are important in studying patients with cholecystitis, particularly in the intervals between acute episodes. The incidence of calculi in nonvisualized gallbladders is extremely high, especially if the common errors in interpretation are carefully screened. Perhaps the most common error concerns the administration and absorption of the dye. Conditions in the gastrointestinal tract that can interfere with absorption include pyloric and intestinal obstruction, hyperacidity, active duodenal ulcer, increased motility and diseases of the small bowel. Diseases of the liver parenchyma and obstructive lesions of the hepatic and cystic ducts will prevent dye from reaching the gallbladder. During an acute attack of cholecystitis a scout film of the gallbladder region without the dye may reveal an opaque stone or, rarely, the presence of gas in the gallbladder. A gallbladder well filled with dye and showing no stones practically excludes gallbladder disease. Poor concentration of dye in the gallbladder without demonstration of stones may be difficult to interpret.

The differential diagnosis of cholecystitis can be very difficult. In addition to considering other diseases of the gallbladder and biliary tract, and diseases of the pancreas, liver and gastrointestinal tract, conditions entirely outside the gastrointestinal tract may produce confusing pictures.

Paroxysmal abdominal pain which may be a form of epilepsy occurs quite frequently in children and may persist into adult life. The condition has been referred to as abdominal epilepsy and probably represents a thalamic dysfunction. At times the syndrome may resemble acute cholecystitis.

Case Reports

Case 1—A. R., a married woman aged 42, was first seen in 1951. She stated that at the age of 16 she began to have severe attacks of nausea and vomiting. The attacks consisted of belching, a sense of bloating, pain in the right shoulder region, nausea and vomiting. Pain was not particularly prominent at the onset of an attack, but after two or three days the abdomen became quite sore. The duration of the symptoms was usually about 36 hours, during which time she was unable to retain even fluid. At first the attacks were infrequent, perhaps one or two a year, but gradually they increased in frequency. The patient was convinced that her attacks were unrelated to food intake or to emotional situations.

In 1939 she was diagnosed as having chronic cholecystitis and cholelithiasis, apparently without the aid of a cholecystogram. Surgery was accordingly performed and the gallbladder removed. The pathologist's report on the surgical specimen read as follows:

"Specimen consists of a gallbladder measuring 7 cm. in length and about 2 cm. in diameter at the fundus. Peritoneum covering the gallbladder is thin, about 1 mm. thick. Mucosa shows a normal honeycomblike structure, reddish tan and is not fixed to the underlying tissue. Gallbladder contains a small amount of dark greenish-brown bile. No stones are present."

This description is consistent with that of a rather normal gallbladder.

The patient continued to have episodes of distress at increasingly frequent intervals. During the six weeks prior to my first observing this patient, she had six episodes of severe nausea and vomiting, resulting in marked debility and loss of weight. Physical examination and laboratory tests, including an x-ray of the gastrointestinal tract, were entirely normal. An electro-encephalogram made at this time was reported as follows:

"Low voltage irregular 7 to 12 per second activity. Generalized random 3 to 4 per second waves or random slowing alternating in either occipital-temporal areas. Slowing increases on hyperventilation. Impression: Record suggests that a convulsive disorder is present."

A diagnosis of abdominal epilepsy was made and the patient was placed on DILANTIN SODIUM.® Her attacks ceased promptly and except for two minor episodes she has been in good health for the past three years.

Patients with abdominal epilepsy usually have a long history of attacks of nausea and vomiting. These attacks often begin in childhood, are widely separated at first, but may become distressingly frequent. Pain may be present but is often a less prominent symptom than in acute cholecystitis. It may be located almost anywhere in the upper abdomen and is perhaps most frequently noted in the umbilical region. The most important feature of the attack is the suddenness of the onset. Patients may feel perfectly well, carrying on their usual routine, and suddenly find themselves in the throes of a severe bout of pain, nausea and vomiting. The attacks may last only a short period or may continue for a few days. Between the attacks there is an absence of the dyspeptic symptoms so often associated with cholecystitis. The upper abdomen becomes tender and may present some resistance after a prolonged attack. Cholecystograms are characteristically normal.

Unfortunately, the episodic character of the pain and vomiting together with the failure to discover an adequate cause has in some instances led to a cholecystectomy on the presumptive diagnosis of a sluggish gallbladder, nonvisualized calculus or biliary dyskinesia. Needless to say, the attacks continue. The diagnosis can be made from an electro-encephalogram and confirmed by controlling the attacks with analeptic drugs. Sudden episodic attacks of nausea, vomiting and upper abdominal pain with normal cholecystograms and negative physical findings are sufficient indications for considering this syndrome.

Unstable psychoneurotic individuals may present a puzzling picture of upper abdominal pain, nausea and vomiting that will tax the skill of any physician.

Case 2—R. O., a married white woman aged 45, was admitted to Mercy Hospital with a possible diagnosis of chronic cholecystitis. She had undergone three pelvic surgical pro-

cedures and had had two postoperative hernias repaired between 1943 and 1949. Following her last operation in 1949, the patient developed a severe emotional disturbance for which she received shock therapy. Neurotic traits, such as persistent enuresis and periodic attacks of pruritus vulvae and pruritus ani, were reported by the patient.

For three years prior to entering the hospital, the patient complained of attacks of right upper quadrant and interscapular pain, belching, bloating, nausea and vomiting. Her family physician saw the patient in many of these attacks and stated that although the patient was writhing in pain, her pulse was always normal and she never had any fever. Morphine did not afford the patient much relief. The attacks occurred at variable periods of weeks to months and usually lasted for only a few hours. She had had at least two complete x-ray studies of the gastrointestinal tract and four cholecystograms made in different hospitals and laboratories. All these procedures were reported as normal. During the three months before admission her attacks had become more numerous and severe. Between the episodes she complained of belching and bloating.

Consultation was requested by the family physician to determine the advisability of surgery in this patient. She seemed extremely anxious and stated that the sooner she was operated on the better, because she could not go on having terrible attacks of pain. Physical examination was essentially negative except for the abdomen. On very light palpation of the right upper quadrant, the patient evinced excruciating pain, wept and otherwise demonstrated a rather severe emotional reaction. The abdomen was alternately soft and defensively rigid according to whether the patient's attention was directed away from herself or not. It was very obvious that her reaction to physical examination of the abdomen was markedly exaggerated.

Laboratory findings and a recent cholecystogram were all within normal limits. Accordingly it was felt that this patient's symptoms were the product of a severe psychoneurosis, and psychiatric consultation was advised. Two days later she was examined by a psychiatrist whose report read as follows:

"Patient had electroshock therapy four years ago and since then has had psychiatric treatment at a clinic. With her past and present history of emotionalism one is not anxious to jump into surgery, but I have a strong feeling that we may be dealing with a somatopsychic problem rather than a psychoneurotic one. It is possible that she has become emotional (attacks of anxiety) because of a basic underlying gallbladder pathology. I would suggest a course of conservative medical management."

Three days later the patient developed typical hysteric manifestations and the psychiatrist advised psychiatric treatment.

Psychoneurotic patients usually present a long history of continued complaints referable to the gastrointestinal tract. As with this patient, they may possess psychoneurotic traits or have had previous severe episodes of nervous instability. The attacks are more closely associated with periods of stress and fatigue than with any form of dietary indiscretion. The symptomatology is often greatly exaggerated and confused by emotionalism.

Physical findings may suggest gallbladder disease by their location but usually they are more diffuse than localized. Frequently the patient's reaction to palpation over the gallbladder is far out of proportion to the pressure applied. In this patient the mere placing of the hand on her abdomen caused her to weep and to react as though she were experiencing great pain.

Neurotic patients presenting a picture of acute cholecystitis in the presence of a normal cholecystogram should be given the benefit of psychiatric consultation and treatment before surgery is seriously considered. Such patients are extremely distressed when removal of the gallbladder fails to alleviate the attacks.

It must, however, be recognized that some emotional individuals may actually have a biliary dyskinesia which may be causing pain. This condition in effect is a disturbance of the normal reciprocal contractions and relaxations with the sphincter of Oddi. The sphincter remains spastically closed as the gallbladder

contracts thereby markedly increasing intraductal pressure. Bachrach, while studying the effects of drugs on intraductal pressure by means of a T tube in the common duct, observed a marked increase in the intraductal pressure in an emotional patient obviously disturbed by the sight and thought of a hypodermic injection. The pressure increase was sustained and similar to that produced by morphine sulfate, a drug known to produce spasm of the sphincter of Oddi. If this diagnosis is strongly suspected, surgery to eliminate sphincter spasm may be considered.

Treatment

The treatment of cholecystitis with cholelithiasis is cholesystectomy. In acute cholecystitis surgery should be done within the first 48 hours or postponed until the acute manifestations have subsided. An exception must be made with the patient whose symptoms and findings are progressing and whose leukocyte count is increasing. Such patients may be developing empyema and should have the benefit of gallbladder drainage.

In chronic cholecystitis with cholelithiasis surgery offers almost certain relief from most of the symptoms, particularly the episodes of pain. In the absence of calculi cholecystectomy may not yield spectacular results. Nevertheless, cholecystitis with or without calculi is an indication for surgery. Recurrent attacks of cholecystitis, cholangitis, hepatitis, pancreatitis and particularly the possibility of malignant disease of the biliary tract and pancreas emphasize the wisdom of removing a diseased gallbladder as soon as possible.

Medical management of cholecystitis is often necessary when surgery is temporarily or permanently contraindicated. In acute cholecystitis the patient should be placed at bed rest. Food and water should be withheld and if vomiting persists, gastric suction can be employed. Parenteral fluid must be used to supply glucose as well as electrolytes and water. Many patients who are unable to retain food and water for two or three days and who vomit constantly will lose large quantities of sodium, potassium and chloride. For pain, morphine or DEMEROL® is usually required. With either of these drugs it is well to employ atropine which tends to counteract the tonic effect which they have on the sphincter of Oddi.

The use of antibiotic substances in acute cholecystitis is generally of little value. Whether or not antibiotic drugs reach the gallbladder depends on the integrity of the liver parenchyma and the patency of the cystic duct. In acute cholecystitis, liver function is undoubtedly somewhat disturbed and the patency of the cystic duct is almost certainly limited. If antibiotics are used one of the broad spectrum types, such as AUREOMYCIN,® should be employed. Perhaps it might be well to restrict use of antibiotics to those patients demonstrating widespread toxic and systemic symptoms.

Chronic cholecystitis does not lend itself to satisfactory medical management. Many patients will be asymptomatic except for occasional acute episodes. Others will have more or less constant dyspeptic symptoms. Dietary regulation is the most important part of medical control. The diet must supply adequate calories while limiting the intake of fats and rich spicy foods. Dairy fats are reasonably well tolerated. Animal fats and greasy foods should be reduced to a minimum.

Bile salts are often employed as a sort of replacement therapy. It is hoped that by increasing the bile salt content of the bowel, digestive processes may be enhanced and intestinal motility improved. This should tend to diminish some of the dyspeptic symptoms.

Saline cathartics administered in hot water before breakfast often decrease flatulence and bloating. Antispasmodic drugs and sedatives may be of value where pylorospasm or colonic pain are prominent features.

Conclusion

Probably the most common cause of dyspeptic symptoms is cholecystitis. In addition, its course may be punctuated with attacks of upper abdominal pain, nausea and vomiting. The etiology of cholecystitis is not primarily bacterial, but late in the history of the disease infection undoubtedly plays a role. Because of the serious complications of cholecystitis,

surgical removal of the gallbladder is the only justifiable treatment. Whether surgery is performed during an acute attack or during a quiescent interval depends largely on the skill and judgment of the surgeon. Medical management may be used to prepare a patient for surgery or to treat permanently unsatisfactory surgical risks. To avoid unnecessary surgery such syndromes as those resulting from psychoneurosis and abdominal epilepsy must be considered.

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Focal Infection and Diseases of the Skin

CARL T. NELSON*

College of Physicians and Surgeons, Columbia University, New York City

CARL T. NELSON

For the purpose of this discussion focal infection is defined as any primary source of microbial infection which leads to the development of secondary lesions. Under this definition, focal infection includes any secondary or distant lesion resulting from the actual metastatic spread of microorganisms from an original focus. What is perhaps more important, it also includes any secondary lesion resulting from the dissemination of nitrogenous microbial products from a focus in a body that has acquired a tissue hypersensitivity or an altered tissue reactivity to those products. Thus the tuberculids, which we identify in the skin as secondary manifestations of a tuberculous process in the lungs, or the vesicular phytids on the palms and fingers of a patient with a severe fungus infection of the feet, are just as much manifestations of focal infection as perinephric abscesses following an attack of boils or subacute bacterial endocarditis occurring after extraction of focally infected teeth from a rheumatic patient.

What is the clinical importance of focal infection in diseases of the skin? Does it play a significant role? Opinions of experienced dermatologists vary from the view that focal infection frequently is an important underlying factor in a large number of dermatoses, to the view that there are very few, if any, dermatologic conditions in which it is of any real importance or as one dermatologist puts it, "One should always *think* of focal infection but never believe in it."

Why does this wide difference of opinion exist? Physicians who readily admit the validity of the concept of focal infection in *acute* situations, such as the gonococcal arthritis which follows an attack of gonorrhea, often reject the idea that microbes or their nitrogenous products can enter the circulation from a *long-standing*, chronic site of infection and

*Professor of Dermatology, College of Physicians and Surgeons, Columbia University and Director of Dermatology, Presbyterian Hospital, New York City.

TABLE 1

MECHANISMS OF FOCAL INFECTION

1. Microorganisms from focus	→	blood and/or lymphatics	→	remote lesions
2. Microbial products from focus	→	acquired tissue hypersensitivity	→	remote lesions
3. Microbial products from focus	→	prepared skin site	→	Shwartzman-like effect
4. Microbial products from focus + host tissues	→	altered antigenic tissue complexes ↓ inflammatory tissue changes of autosensitization	⇄	auto-antibodies

set up a secondary disease process in other regions.

There are probably several reasons for this state of affairs. First, there are the excesses committed in former years, when any structure harboring microorganisms was called a "focus" and was indiscriminately assigned an etiologic role in any disease that happened to coexist in the patient. Secondly, many patients with diseases allegedly caused by chronic focal infections have not been relieved of their symptoms by removal of the foci. And finally, patients with the same clinical condition may not all show evidence of focal infection or, conversely, demonstrable chronic foci of infection may be as common in apparently healthy individuals as in those with disease.

On the other side of the picture, however, we must emphasize that the mere removal of a focus may not eliminate the disease it started or reverse the permanent tissue changes which may have occurred. Certain accessory or conditioning factors, such as alterations in tissue immunity, local disturbances of blood supply, tissue anoxia, etc., may produce permanent changes which render the patient vulnerable to microbial products from a focus which otherwise could be borne without difficulty. Moreover, the fact that undoubted chronic foci of infection exist in many patients without causing distant ill effects does not prove that foci are incapable of producing disease. It merely proves that foci alone, without the accessory or conditioning factors, may not be sufficient to produce any obvious secondary disease.

On logical grounds then, the basic theory cannot be entirely discarded. It is still valid theoretically, and there is some good experimental evidence to support the idea, even though dermatologists find that absolute proof of the role of a chronic focus in a given dermatosis is frequently lacking. Under these circumstances, it is worthwhile to examine again possible mechanisms by which chronic microbial foci may establish distant skin disease.

Possible Mechanisms

A chronic focus of infection may initiate or affect the course of a distant, secondary manifestation in one or more of four main ways (table 1).

1. Microorganisms may be discharged from a focus into the blood or lymphatics and set up secondary lesions directly. This "metastatic" type of focal infection is found, for example, in bacterial endocarditis following dental infection. Here the important conditioning factor seems to be the previous local damage to the heart valve which permits localization of otherwise rather innocuous microbes (*Streptococcus viridans*) from the distant dental focus. This mechanism is rarely encountered in dermatologic conditions.

2. The nitrogenous products of microbial metabolism in a focus may reach and damage remote parts of the body. If the tissues have become sensitized to these substances in the

allergic sense, then continued liberation of the microbial products may result in distant tissue reactions. Dermatophytids and tuberculids belong in this category.

3. Another mechanism of focal infection which may be of importance in dermatologic disease is the possibility that a Shwartzman-like reaction may be elicited at a previously prepared skin site by nitrogenous products emanating from a primary microbial focus. For example, a chronic, secondarily infected stasic dermatitis may serve as a previously prepared skin site which may be kept in a persistent state of nonspecific exacerbation by nitrogenous materials produced as a result of microbial metabolism in a distant primary focus. The microorganisms present in the focus need not even be closely related to the species present in the stasic dermatitis. This Shwartzman-like effect, or lighting up of a previously prepared inflammatory site in the skin by the absorption of nonspecific microbial products elaborated in a primary nidus, is a concept of focal infection which has not been stressed in dermatologic literature. It is one that seems to deserve some emphasis.

4. There is experimental evidence that certain microorganisms, particularly staphylococci and streptococci, in secondary localizations may react with the host's own tissues to render them antigenic in the sense that antibodies may be produced in the host against his own altered tissue components. On interaction with the involved tissue, these antibodies will produce inflammatory changes. In this situation, elimination of the focus may prevent the formation of more antigenic complexes, but it cannot be expected to eliminate the permanent tissue damage already done by the auto-antibodies. Thus the focus may be only a small link in a chain of events largely determined by other conditioning factors. Often the focus does not play the whole etiologic role and its elimination at a late stage in the course of a disease may not give a clinical cure.

These seem to be the more important possible mechanisms of focal infection. Our understanding of them is less than complete and this may partly account for the reluctance of many physicians to accept the concept. Actually, although the source of trouble is basically an infection, in dermatologic conditions the clinical consequences are rarely due to metastatic spread of the microbial agent itself. More commonly they are the result of an allergic response of sensitized tissue to the various microbial products released from the focus. As has been suggested, perhaps the term "focal allergy" would be preferable.

Establishing the Etiologic Role of Focal Infection

In diseases of the skin, absolute proof of the role of an infectious focus in a given case is difficult to establish. It is virtually impossible to state with certainty that a focus of infection is related to a particular patient's symptoms. For the most part, the evidence that an infectious focus may play a role in a certain condition consists of single case observations of clinical improvement after removal of a suspected focus. Opponents of the theory of focal infection claim that this evidence is not significant and that such improvement may well be fortuitous. They emphasize the cases in which the removal of a suspected focus did not improve the clinical condition.

Conclusive proof that focal infection is related etiologically to a given dermatologic condition would have to embody certain points: (1) It should be shown that removal of the microbial focus is more often than not followed by distinct improvement or cure of the dermatologic disease; (2) the suspected focus should yield a microbial agent which in itself or through the products of its metabolism may produce distant effects, especially in the hypersensitive patient; (3) it should be possible to reproduce or precipitate the clinical condition by readministration of the microorganisms or their products in the patient.

Few cases showing such a chain of evidence are known to us or are to be found in the literature. However, when this type of proof can be obtained it is quite impressive. Recently it has been shown that erythema annulare centrifugum may occur in a sensitized individual as a distant manifestation of

a proved focus of *Trichophyton* infection of the toe webs.* In this instance, the fungus was isolated and clearing of the dermatophytosis of the feet was followed by disappearance of the erythema annulare centrifugum. Reinoculation of the fungus culture into the toe webs and re-establishment of the dermatophytosis were followed by a return of the erythema annulare centrifugum. The distant skin eruption could again be abolished and reproduced by eradication and experimental production of the tinea pedis. This is the type of evidence needed to convince more physicians that a primary focus is etiologically related to a distant dermatologic condition. Unfortunately, proof of this sort can be obtained only rarely.

Dermatoses Related to Focal Infection

The dermatologic conditions in which focal infection appears to be of some significance are listed in table 2. The opinions of several dermatologists, reports in the literature, and personal experience have been used to compile the table. Those who reject the idea that focal infection may play a role in diseases of the skin will find the list too long. Others who are in favor of the concept will find it inadequate and incomplete. Indeed, there are those who believe that focal infection may also be of consequence in lupus erythematosus, acute attacks of psoriasis, acne vulgaris, dermatitis herpetiformis, atopic eczema, nummular eczema, prurigo aestivalis, rosacea, alopecia areata, furunculosis, dermatomyositis, lichen planus, anogenital eczema and pyoderma gangraenosum.

TABLE 2

DERMATOSES RELATED TO FOCAL INFECTION

FOCAL INFECTION OF ETIOLOGIC SIGNIFICANCE
Tuberculids
Syphilids
Dermatophytids
Bacterids (Andrews)
FOCAL INFECTION OFTEN SIGNIFICANT
Localized bullous eruptions (S. Epstein)
Infectious eczematoid eruptions—ears, hands, legs
Angio-edema and chronic urticaria
Erythema multiforme
Erythema nodosum
Simple purpura

In conclusion, it seems fair to say that the importance of focal infection in diseases of the skin remains a controversial subject. However, the last 20 years have brought better understanding to the problem, with the result that the concept seems to be regaining some respectability. One may predict that as further clarification of the problem takes place and its mechanisms are more fully understood, more physicians will conclude that there is something to the concept of focal infection after all.

*JILLSON, O. F. and HOEKELMAN, R. A.: Further amplification of the concept of dermatophytid. Arch. Dermat. & Syph. 66:738, 1952.

SCIENTIFIC EXHIBIT

Cervical Disk Lesions

LEE T. FORD AND J. ALBERT KEY

Washington University School of Medicine, St. Louis

The purpose of this exhibit is to point out that we believe cervical disk lesions are much more common than is usually thought; and further, that this condition may nearly always be treated adequately by conservative measures, but may require conservative treatment in a hospital. Only rarely is myelography and surgical removal of the disk necessary.

Key Points in History

1. Presence or absence of an injury, either recent or remote.
2. Usually a history of recurrent episodes of cervical pain with or without referred pain to the upper extremity is present.
3. There is usually some pain in the scapular region.
4. Occipital pain with headaches may be present.
5. Referred pain to the shoulder is often present or associated with these lesions.
6. Pain may be referred down the upper extremity and is usually present on one side, but may be present on both sides.
7. There may be a history of numbness or paresthesia in the upper extremity.
8. Actual muscle weakness may be, but is not often present in the upper extremity.
9. Actual spastic paraplegia can be produced by a large midline lesion, but is rare.

Physical Findings

1. A varying degree of limitation of neck motions is usually present (figures 1 to 4).
2. Pain in the neck or in the upper extremity may be aggravated by neck motions and by impaction of the head on the neck, especially when the head is held in extension (figure 8).
3. Relief of this impaction pain is usually obtained by applying traction to the head (figure 9).
4. Local tenderness may be present in the neck and most marked over the involved interspace (figure 5).
5. Tenderness in the scalene triangle on the affected side is often present (figure 6).
6. Diminution or absence of triceps or biceps reflex may be, but is not often present (figure 7).
7. Hypesthesia of a dermatome pattern may be present in the upper extremity, especially in the hand.
8. Loss of muscle power may be, but is not often present in the upper extremity.

FIGURE 2. Next, the extension is determined.

FIGURE 1. The first step in examining is to obtain the range of forward motion or flexion.

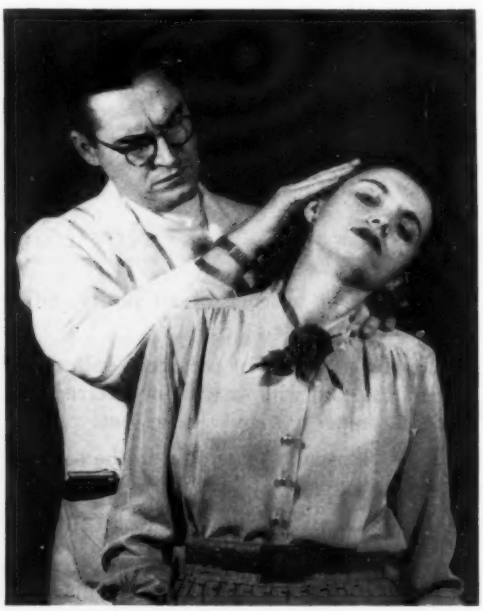


FIGURE 3. The range of lateral motion in each direction is tested.

FIGURE 4. Rotation in each direction is similarly tested.

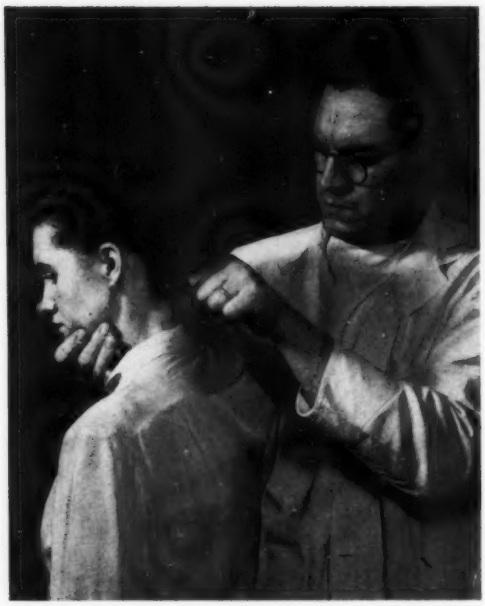


FIGURE 5. Tenderness in the posterior cervical region is tested.

FIGURE 6. Tenderness in the scalene triangle is often present.

FIGURE 7. The biceps and triceps reflexes are tested.

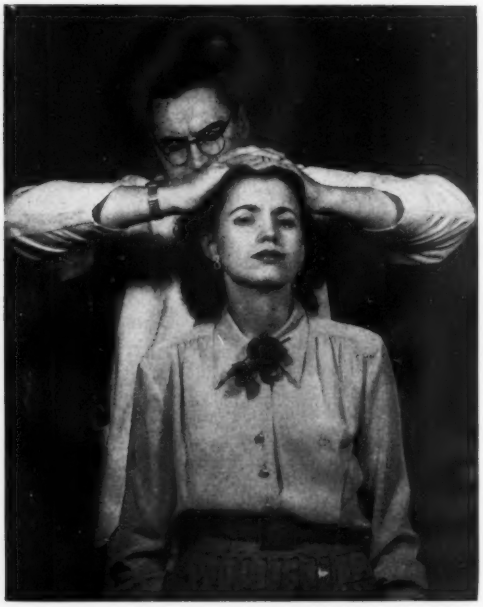


FIGURE 8. Impaction may aggravate the neck and the radicular pain.

FIGURE 9. Traction, on the other hand, often relieves the pain.

X-Ray Findings

1. There may be no abnormal x-ray findings but in an acute cervical disk, loss of or a reversal of the lordotic curve is frequently seen (figure 10).
2. Narrowing of the involved intervertebral space may be present (figure 11).
3. There may be spurring of adjacent vertebral bodies (figure 12).
4. Sclerosis of the adjacent portion of the involved vertebral bodies may be present in old disk lesions.
5. A defect in a cervical myelogram is evidence of a ruptured cervical disk. (The myelogram should be performed only when surgery appears necessary—figure 13.)
6. Other laboratory findings have no significance.

FIGURE 10. Reversal of the normal cervical lordotic curve in association with a cervical disk lesion.

FIGURE 11. Typically narrowed disk space between fifth and sixth cervical vertebrae.

FIGURE 12. Marked spurring at the posterior part of narrowed disk between fifth and sixth cervical vertebrae.

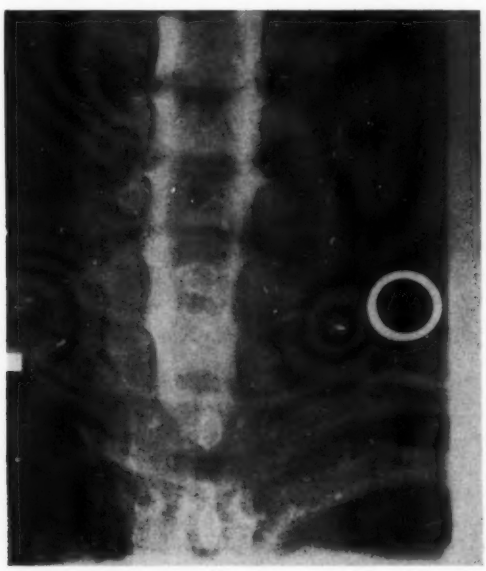


FIGURE 13. Myelogram of the cervical spine, anterior view. There is a small defect on the right between the sixth and seventh cervical vertebrae. This was removed at operation and the symptoms were relieved. Rarely is a myelogram indicated unless surgery is contemplated.

Treatment

1. The majority of cases may be treated in the home, office or hospital by:

   a. The use of head traction at home using 5 to 10 pounds for 15 to 20 minutes two or three times a day (figure 14).

   b. The wearing of an individually fitted Thomas collar (to be worn most of the time the patient is not in bed—figures 15 and 16).

   c. The use of head traction (20 to 50 pounds) in the office for a short period of time combined with gentle manipulation once or twice a week (figures 17-19).

   d. Suitable medication such as salicylates, barbiturates, vitamin B complex, vitamin B_{12}, occasionally opiates and cortisone (in a few cases deep x-ray therapy may be useful).

   e. The use of an extra pillow when sleeping.

2. More severe cases may require treatment in the hospital by prolonged head traction in bed (figure 20).
3. Operative removal of the ruptured disk is rarely necessary.
4. Fusion of the cervical spine is very rarely indicated.
5. Careful diagnostic study including x-rays should be carried out in every case so that the manipulation as described is not done where it might be harmful or even dangerous (figures 21-24).

Traction Apparatus

The apparatus for using head traction in the home is simple. A Sayre halter, a spreader, two pulleys, rope and a 5 to 10 pound weight are necessary. The two pulleys may be placed in a basement joist, or in the top of a door frame (figure 14).

The traction apparatus used in the office is similar except that a block and tackle is used to apply traction and the rope is anchored while manipulation is carried out.

FIGURE 14. Head traction in use at home.

The Thomas Collar

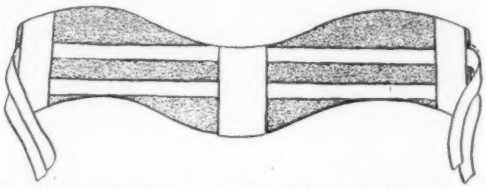
(Figures 15-16)

This type of Thomas collar may be made in the office and fitted to the individual with simple materials. The basic material is an electrical "pressboard" which is obtainable in large sheets from lumber or building supply companies. This is cut until it fits comfortably around the patient's neck.

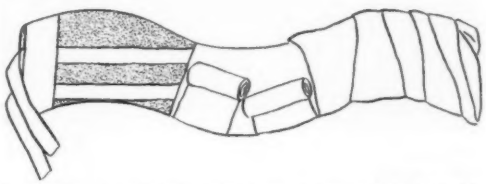
Two strips of bias tape are held in place by adhesive tape. Sheet cotton or absorbent cotton is used to pad the collar. This padding is held in place by a roller bandage. Ordinary four-inch stockinette is used for a cover.

This cover may be washed daily. The collar is tied in place by tapes. It is removed for meals, for bathing and for sleeping.

This original pattern is cut for the individual and held around the neck and trimmed until a proper fit is obtained.



Two strips of bias tape are applied and held in place with adhesive tape.



The collar is padded with sheet cotton which is held in place by roller bandage, and then covered with stockinette.

FIGURE 15. The Thomas collar from the front.

FIGURE 16. The Thomas collar from the side.

FIGURE 17. Traction may be applied in the office or in the hospital.

FIGURE 18. With traction maintained the neck may be manipulated laterally in each direction.

FIGURE 19. The neck is also rotated in each direction.

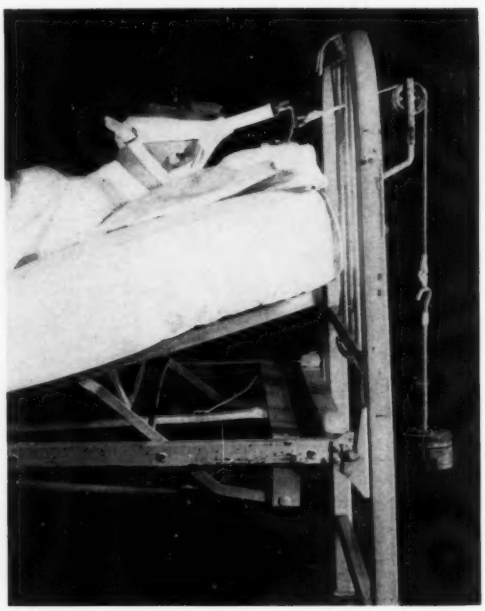


FIGURE 20. Continuous traction, in the hospital.

FIGURE 21. A cervical subluxation with a fracture of the odontoid such as this would not be forcefully manipulated. There is slight forward displacement of C_1 and C_2.

FIGURE 22. A fracture-dislocation of the cervical spine would not be manipulated in the manner described. C_3 is displaced forward on C_4.

FIGURE 23. A cervical spine showing metastatic carcinoma such as this should not be manipulated. Osteoblastic areas scattered through the cervical spine are the areas of tumor.

FIGURE 24. A tuberculous spine such as this should not be manipulated. The body of C_6 in this child has been almost completely destroyed.

Editorials

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THERAPY OF CARCINOMA OF THE CERVIX UTERI

THERE seems to be little if any ground for considering radiation therapy and surgical management of carcinoma of the cervix to be in competition. There are indications for each of these forms of treatment, and in some cases a combination of the two serves the best interests of the patient.*

Following the work of Clark, Rumpf, Emil Reis, and Wertheim in the latter years of the last century, radical abdominal hysterectomy was the accepted method of treatment of operable cases throughout the world. The absolute five-year survival rate was not over 25 per cent. Extensive cases were treated palliatively by curettage, cauterization and the application of various caustic preparations.

After the advent of radium, the majority of surgeons abandoned operative treatment because of its high immediate mortality. Thirty per cent of Wertheim's first 100 patients failed to survive the operation; this rate was reduced to 15 per cent in his later cases. It is estimated that the average mortality rate of the radical operation during the height of its employment was approximately 20 per cent, and even this staggering figure does not take into consideration the large number of women who were doomed to invalidism by postoperative urinary and rectal fistulas.

In 1912, Kelly and Burnham of Baltimore initiated the elective treatment of carcinoma of the cervix with radium. The negligible primary mortality, the low incidence of post-treatment morbidity, the almost miraculous immediate response, and the high incidence of apparent cures resulted in its adoption as the treatment of choice in most of the major gynecologic clinics throughout the world.

The technic of radiation therapy has undergone a gradual evolution during the past 40 years. With the increase of knowledge of the physics of radiation and the biologic reaction of tissues to this form of therapy, it is rare indeed to see the needless destruction of tissue which was formerly referred to as "the usual radium slough." In most clinics at the present time treatment with high voltage roentgen rays precedes the local application of radium. This has the advantages of (1) devitalizing the cancer cells before local manipulation can cause their dissemination; (2) at least partially sealing lymphatic channels; (3) clearing up the ever present local infection; and (4) effecting an amazing restoration of cancer-distorted anatomic relation-

*A report of the procedures followed at the Mayo Clinic will be found in the article by Dr. Joseph H. Pratt, page 483, this issue.

ships, thereby permitting more accurate local application of radium.

A fair average of five-year salvage following good radiation therapy for growths apparently limited to the cervix is 75 per cent; for those questionably limited, it is 50 per cent; for those which have invaded the broad ligaments, it is 20 per cent; and in the group of cases in which the growth has involved the entire pelvis, the five-year salvage is practically nil. These results, reported by a large number of gynecologists and radiologists, are comparable to the salvage obtained by only the best surgeons with the radical operation. It is interesting to note that these survival rates are in direct proportion to the usually recognized absence of involvement of the regional lymph nodes in the various stages of the disease. This brings clearly into focus the necessity of more effective technics of radiation or surgical removal of the metastatic nodes.

Over a period of years increased doses of both radium and roentgen rays have resulted in a steady increase in five-year survival. This increased dosage has, at the same time, unfortunately caused an increase in the incidence of untoward postradiation complications. Among these are early cystitis, proctitis, inflammatory reactions in the genital tract, late atrophic ulcers of the bladder and rectum, stenosis of the bowel, and ureteral obstruction. While this array of sequelae seems formidable, serious complications are encountered in not more than 10 per cent of cases. Further, the incidence of complications can be lowered by more accurate placement of radium applicators, by their maintenance in proper position throughout the period of treatment, by giving the bladder and bowel the protection of distance with proper vaginal packing, and by avoiding overdosage to the structures in the center of the pelvis. Checking the position of the radium by roentgen ray studies immediately after application is essential for safety and for calculation of the tissue dosage. In planning radiation therapy we must give up thinking in terms of an arbitrary number of milligram hours in favor of calculating tissue dosages to be delivered to specific points in the pelvis. From 7000 to 12,000 gamma roentgens are found to be cancerocidal.

Considerable controversy exists concerning the value of radiation therapy of cancer which has already extended to regional lymph nodes. Taussig concluded both from his own experience and from an extensive review of the subject that radiation therapy did not destroy metastases in lymph nodes; for this reason he developed his technic of lymphnodectomy as an adjunct to full radiation therapy. By this method he was able to increase his five-year salvage from 22.9 per cent to 38.6 per cent in groups of cases of comparable extent. On the other hand, Morton found cancer in lymph nodes three times more often in patients who had not received preoperative roentgen ray therapy than in a comparable group who had been so treated. This indicates that present methods of radiation therapy can in some cases destroy cancer in lymph nodes. This is further suggested by the improved salvage reported by many clinicians following the use of modern methods of roentgen ray therapy.

During the past decade a few of us in this country returned to the radical Wertheim operation combined with regional lymphnodectomy for the treatment of certain early selected cases of cervical carcinoma. The reasons for this return to the surgical approach were: (1) to prevent recurrence locally by removal of the cervix; (2) the fact that certain tumors are radiation resistant; (3) the hope of salvaging a certain percentage of patients who already have lymph node metastases; and (4) the avoidance of untoward radiation injuries to surrounding structures.

More than two-thirds of cases are so far advanced that radical hysterectomy is not possible. To be of any value the operation must consist of removal of the entire uterus, the upper half of the vagina, both tubes and ovaries, the entire parametrium, and sacral, obturator and iliac lymphnodectomy as far as the bifurcation of the aorta. The ureter must be freed from the parametrium and all surrounding areolar tissue. Any hysterectomy for invasive cervical carcinoma which is less extensive in scope must be branded as meddlesome, ineffectual and dangerous. Unfortunate-

ly, the publicity which some of us have given the return to the surgical approach has resulted in a tremendous increase in the number of inadequate operations for cervical carcinoma. Not only does such an operation fail to eradicate the disease, but even worse, it lessens the opportunity of salvage by radiation therapy.

Illustrative of the treachery of this disease is a recent patient on our service. Mrs. C. P. had slight postmenopausal vaginal bleeding for two weeks; she reported this to her physician who immediately performed a biopsy and conization of the cervix; epidermoid carcinoma was found. She was sent to us one week later at which time a repeat biopsy was negative. Radium was applied. On follow-up examination one month later the cervix appeared to be normal. The vaginal vault was so narrow that a proper vaginal application of radium could not be made. For this reason radical hysterectomy and pelvic node dissection were performed. No residual carcinoma could be found on microscopic study of the cervix; despite this fact, carcinoma was found in the iliac nodes on both sides, and in one node lying to the left of the aorta. This case, more than any other in our experience, illustrates the total inadequacy of ordinary total hysterectomy in the treatment of even minimal invasive cervical carcinoma.

Our own experience with radical hysterectomy leads us to believe that the survival rate is no greater than that obtained by proper radiation therapy in cases of similar extent. The incidence of injury and loss of the lower ureter has increased each year that the operation has been utilized. This is explained by the fact that we have steadily increased the scope of the procedure; greater care has been taken to strip the ureter of parametrial tissue which might be cancer-bearing. In so doing we have done irreparable damage to the ureteral circulation in an increasing number of cases. The radical operation is now, therefore, reserved for occasional special indications and is no longer our elective treatment for even the earliest invasive lesions.

The special indications for surgical management are somewhat varied. We feel that operable carcinoma of the cervical stump is best treated by radical operation because of the danger of damage to the bladder and bowel by the local application of radium. If the vaginal vault is so narrow, as in the case just cited, that the bases of the broad ligaments cannot be given a cancerocidal dosage of radium, radical hysterectomy and node dissection are indicated. We believe the same approach to be indicated in the treatment of early carcinoma complicated by pregnancy. The operative approach deals simultaneously with the pregnancy and the malignant lesion. In certain cases complicated by large uterine myomas or major adnexal tumors, primary radiation therapy is contraindicated. All radical surgical procedures are followed by full external roentgen therapy.

We have found that radical hysterectomy and lymphnodectomy following full radiation therapy entails even greater danger of damage to the ureters and bladder than exists in patients who have not been so treated. The devitalization of tissues incident to radiation renders healing extremely slow and, too often, impossible. Also, the node-bearing areolar tissue, which usually strips easily off the great vessels, is so altered by radiation that clean dissection cannot be performed. The wisdom of attempting radical hysterectomy and lymphnodectomy after full radiation is, therefore, questionable. In cases of failure of proper response to radiation, the more radical operation of exenteration is utilized.

Our own experience with pelvic exenterations is rather limited. Among these there has been but one operative death, the patient dying of massive secondary hemorrhage on her twentieth postoperative day. The procedure has so far been used only after full radiation therapy has failed to control the disease. Its greatest field of usefulness is with patients who develop vesicovaginal or rectovaginal fistulas.

Heretofore, vaginal and rectal examinations have been depended on to make, at best, an estimate of the extent of the growth. Too often such estimates are later found to be inaccurate. Since carcinoma of the cervix in the absence of properly administered treat-

ment is invariably fatal, it seems logical to determine the exact local extent of the process by laparotomy before radiation therapy is begun.

As our present methods of irradiation of the side walls of the pelvis are admittedly inadequate, surgical removal of the regional lymph nodes is imperative. Lymphnodectomy, as noted previously, can be accomplished best before full radiation therapy is given.

It seems reasonable, therefore, that exploratory laparotomy combined with regional lymphnodectomy should constitute the first step in the therapy of cervical carcinoma. This procedure is followed by full external roentgen therapy and the local application of radium into the cervical canal and into the lateral vaginal vaults. Our present methods of application of radium plus the roentgen dosage yield an estimated cancerocidal dosage to structures 4 cm. distant from the midline. Therefore we are depending on the local application of radium to destroy the original lesion and on the combination of lymphnodectomy and external roentgen therapy to eradicate the disease along the lateral walls of the pelvis. This plan was initiated late in 1952; while it is much too early for statistical evaluation, we are encouraged to believe that increased salvage will result.

ROBERT A. KIMBROUGH, JR.

WOMEN IN THE LABOR FORCE

FOR many years the proportion of women, especially married women of all ages, in the labor force has consistently increased. More and more families are now "two pay check" families. Today fewer young people are working in proportion than were available for labor in 1890 and the number of older persons working has increased tremendously.

In the United States about 60,000,000 people work to take care of the needs of the remaining 100,000,000. In 1870, 1.9 million women and 11 million men were working, making about 15 per cent women and 85 per cent men. In 1900 it was 5.3 million women and 23.8 men with about 18 per cent women and 82 per cent men. In 1950 there were 16.5 million women and 43.6 million men working and the percentages had changed to 27.5 women and 72.5 men. The number of men in the labor force has increased four times; the number of women nine times. Today 23 per cent of all married women are employed. Many of the changes that have occurred are due to the introduction of machines which do the heavy work of industry. This change in occupation has, however, had definite reflection in the medical profession and its responsibilities.

The woman in industry constitutes a special problem, modified by her special physiology and pathology. The economics of medical practice are also affected since the "two pay check" family is better able to meet the ordinary needs of living than the family in which only the male is an earner and supports the wife and the children.

MORRIS FISHBEIN

REFERENCE

The Labor Force of the United States. Population Bulletin, Population Reference Bureau, Inc., March 1954.

THE STREPTOMYCIN ANNIVERSARY

THE discovery of streptomycin in 1944 in an obscure and crowded laboratory at Rutgers University was celebrated early this month at Rutgers with the dedication of a new Institute of Microbiology, costing more than $3,500,000. The occasion was marked by a two-day scientific symposium with more than 400 leading scientists participating.

Dr. Selman A. Waksman, winner of the Nobel Prize in medicine and physiology in 1952 and first director of the new Institute, began his studies of *Actinomyces* in 1914. Streptomycin was first isolated from a strain of the microbe in a swab taken from a chicken's throat on August 20, 1943. The announcement was first made in January 1944 and in April of that year the activity of the drug against tuberculosis was demonstrated.

Since that time the effectiveness of streptomycin against tuberculosis has been fully demonstrated and the most spectacular results have been obtained in its use against miliary

tuberculosis, tuberculous meningitis, laryngeal bone and joint tuberculosis. Recent reports indicate greatest usefulness when treatment also includes p-aminosalicylic acid and various forms of isonicotinic acid hydrazide. The supplementary use of these compounds lowers the toxicity of streptomycin and retards the development of resistance to the drug.

The production of streptomycin is now in excess of $100,000,000 annually. In the United States during 1953 nine companies produced between 15 and 20 million grams a month. The royalties from the manufacture of streptomycin, amounting to more than $4,000,000 have been assigned in large part—80 per cent—to the Rutgers Research and Endowment Foundation. From these funds the new building was constructed and equipped. This contribution by Dr. Waksman deserves every possible recognition from the medical profession to whose ideals he has been so fully devoted.

MORRIS FISHBEIN

THE SUPPORT OF MEDICAL RESEARCH

In round numbers, the United States spent $173 million for medical research in 1952—about four times the amount spent in 1940. Of the $173 million, $73 million or about 42 per cent was contributed by the federal government. Irving Ladimer,[1] Assistant Director of the Research Planning Branch of the National Institutes of Health, recently indicated the various trends in medical research that now prevail.

Since the beginning of World War II expenditures for research have increased at a faster pace than general economic activity. However, the number of scientists and engineers has not grown at the same rate as expenditures. Since 1941 medical research expenditures have constituted about one-twentieth of the total outlay for research and development in the United States. Especially impressive is the amount contributed by nonprofit and philanthropic agencies which aid medical research. Before the war the nonprofit groups contributed over one-third of the medical research funds in contrast to 2 per cent for research generally.

In 1947 the government assumed about one-half of the $2.25 billion of support for science research generally and about one-third of the $88 million for medical research. By 1952 the research program consumed about $3.75 billion with three main sources of support: the federal government, industry and nonprofit organizations. The $173 million spent on medical research in 1952 came from the same three principal sources.

The large figure results chiefly from crediting all of the Atomic Energy Commission expenditures for biologic study as contributions for medical research. The amounts contributed by nonprofit organizations have been separated into two groups: foundations, trusts and voluntary organizations on the one hand, and schools, hospitals and similar institutions on the other. Thus of the four participants in 1952, government contributed the largest portion, 42 per cent, and educational and other institutions the smallest amount, 9 per cent. Industry contributed 35 per cent and philanthrophic organizations 14 per cent.

In 1952 contributions by philanthropic organizations for research included more than $5 million for cancer, $1.5 million for heart diseases, $1 million for arthritis and metabolic diseases, $4 million for such neurologic conditions as poliomyelitis and blindness and, finally, a little over $300,000 for mental health.

Few physicians realize the part played by federal funds in supporting research in medical schools. During the fiscal year 1948, about $4.2 million or nearly one-fourth of all expenses for research budgeted separately in the four-year medical schools represented research funds granted by the U. S. Public Health Service. These grants accounted for all of the expenses for separately budgeted research in one school. Thus not only the research function but also the teaching and training functions of the schools have been aided by this form of government support.

MORRIS FISHBEIN

1. Ladimer, Irving: Trends in support and expenditures for medical research, 1941-52. Public Health Reports 69:111 (February) 1954.

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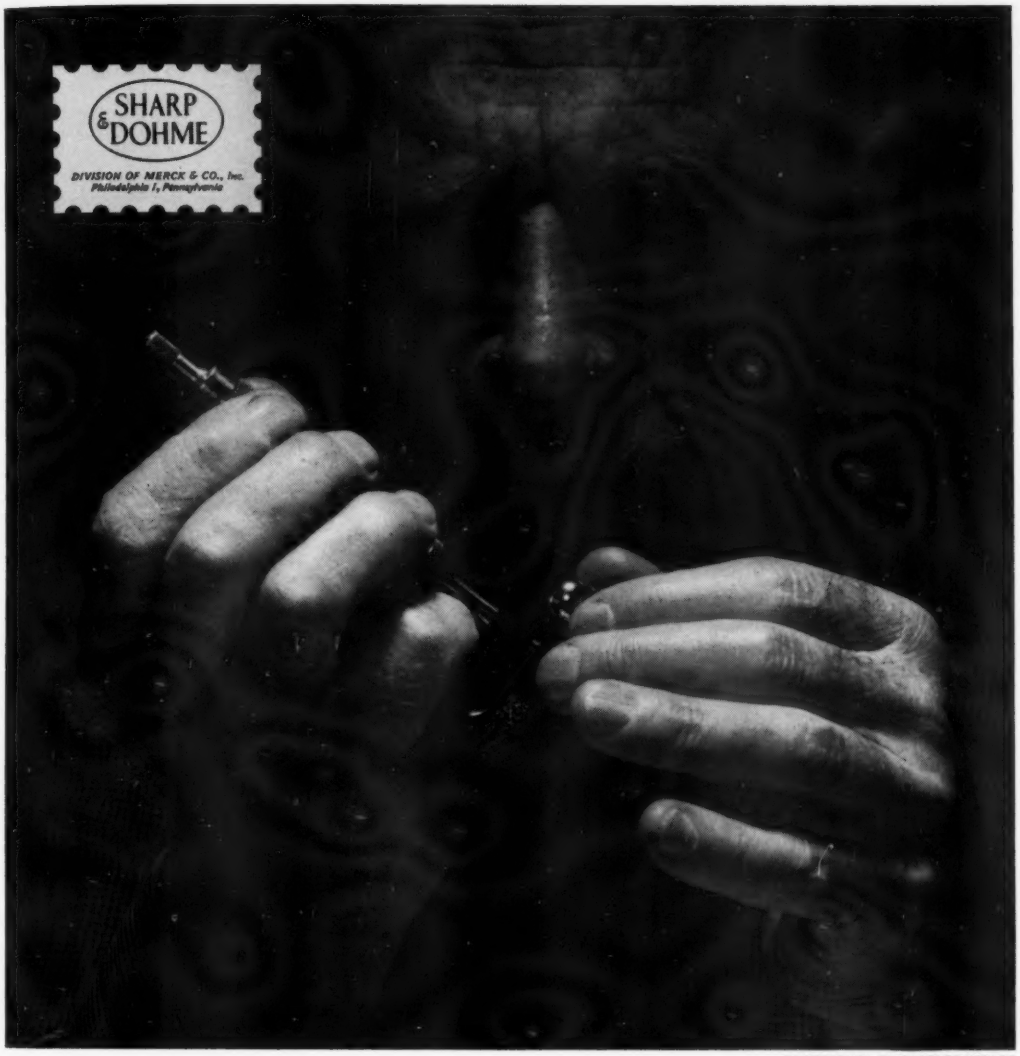

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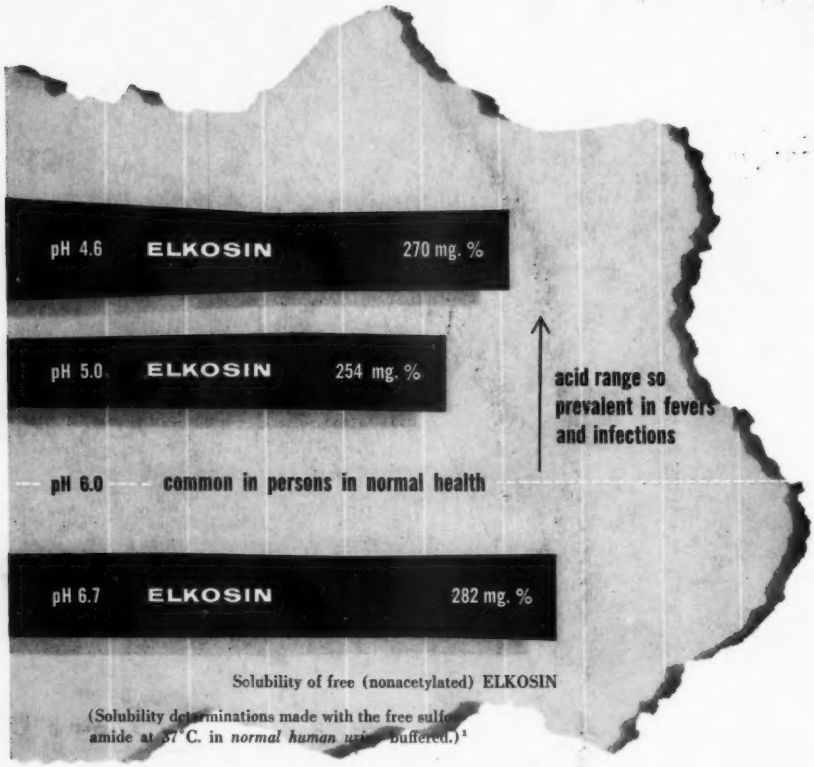
*From a case report: J.A.M.A. 153:191, 1953.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pH 6.0 common in persons in normal health
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high solubility where it counts

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1. Ziegler, J. B.; Bagdon, R. E., and Shabica, A. C.: To be published.

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